SERUM CALCIUM IN NEWLY DIAGNOSED ESSENTIAL HYPERTENSIVES

DISSERTATION SUBMITTED FOR

THE FULFILLMENT OF

DOCTOR OF MEDICINE

BRANCH I – GENERAL MEDICINE

MARCH 2007

THE TAMILNADU DR. M. G. R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

CERTIFICATE

This is to certify that this dissertation entitles **"SERUM CALCIUM IN NEWLY DIAGNOSED ESSENTIAL HYPERTENSIVES"** submitted by **Dr. V.ANAND** to The Tamilnadu Dr. M. G. R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D. Degree Branch I (General Medicine) and is a bonafide research work carried out by him under direct supervision and guidance.

Dr. M. Kamaraj, M.D.,
Additional Professor,
Department of Medicine,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

Dr. N. Nalini Ganesh M.D.
Professor and Head
Department of Medicine,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

DECLARATION

I Dr. V.ANAND declare that I carried out this work on **"SERUM CALCIUM IN NEWLY DIAGNOSED ESSENTIAL HYPERTENSIVES"** at Department of General Medicine, Government Rajaji Hospital during the period of February 2005 to January 2006. I also declare this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M. D. Degree examination in General Medicine.

Govt. Rajaji Hospital **Dr. V. ANAND**

Madurai.

ACKNOWLEDGEMENT

At the outset I wish to thank our Dean **Dr. S.M.SIVA KUMAR M.D.,** for permitting me to carry out this study in our hospital.

I sincerely thank my professor and unit chief **Dr. M. KAMARAJ, M.D.,** for his eminent and continuous guidance in the project work that I was assigned.

I am also thankful to my Assistant Professors in the Department of Medicine, **Dr. S. RAVINDRAN, M.D., Dr.J.SANGUMANI, M.D., Dr. P. MANIMEGALAI, M.D.,** and **Dr.S.AMALRAJ M.D.,** for their constant encouragement, timely help and critical suggestions.

I express my sincere thanks to Prof. **Dr. N. NALINI GANESH, M.D.,** Professor and Head of the Department of Medicine, who guided and encouraged me in various aspects of preparation of this project work.

I thank my **co-postgraduates** for helping me in this study.

Last but not the least, I sincerely thank all those **patients and controls** who participated in this study, for their co-operation.

CONTENTS

INTRODUCTION

Hypertension is one of the leading causes of death and disability among adults all over the world. It remains the major risk factor for coronary, cerebral and peripheral vascular disease. Essential hypertension comprises more than 90% of hypertension[1].

Hypertension is an emerging health problem in India. When majority of people come to know that they have hypertension they have already advanced into a stage with target organ damage – a fatal stroke or myocardial infarction or irreversible renal failure. Unfortunately even in developed countries like United States, fifty million people are found to have hypertension. Of these, 70% are aware of their diagnosis, but only 50% are receiving treatment and only 25% are under control[2].

In addition to a primary increase in cardiac function propelled by overactive sympathetic nervous system, primary retention of salt and water by kidney, other factors contributing to hypertension are hereditary predisposition and high sodium and low potassium intake and excretion.

In a country like India, people used to have a diet rich in sodium and poor in potassium, and calcium. Many studies have shown that a correlation exists between serum calcium and blood pressure. They have shown that a decreased intake of sodium and increased calcium intake or both together may be effective in prevention or even treatment of hypertension.

REVIEW OF LITERATURE

ESSENTIAL HYPERTENSION:

An elevated arterial pressure is one of the most important public health problems and despite it's widely recognized high prevalence and associated danger, it remains inadequately treated in majority of the patients. It is common, readily detectable, and usually easily treatable and if left untreated can lead to serious morbidity and mortality from cardiac, cerebrovascular, vascular and renal disease. Adequate hypertension control remains elusive because of the asymptomatic nature of the disease for the first 15 – 20 years even as it progressively damages the cardiovascular system[3]. Although our understanding of the pathophysiology of hypertension has increased in 90% to 95% of cases, etiology is still mostly unknown[4].

Definition and classification:

Blood pressure is distributed in a typical bell shaped curve within the overall population. As seen in the Multiple Risk Factor Intervention Trial (MRFIT), the long term risks for cardiovascular mortality rise progressively over the entire range of blood pressure, with no threshold that clearly identifies the potential danger. Therefore the definition of hypertension is

somewhat arbitrary and usually taken as that level of pressure associated with doubling of long term risks.

According to JNC (Joint National Committee) 7 report, in adults aged18 years and above, systolic blood pressure of <120 mm of Hg and diastolic blood pressure of <80 mm of Hg is normal. Systolic blood pressure of 120 – 139 mm of Hg and diastolic blood pressure of 80 – 89 mm of Hg is prehypertension. In stage I hypertension, the systolic blood pressure is 140 – 159 mm of Hg and diastolic blood pressure is 90 – 99 mm of Hg. In stage II hypertension, systolic blood pressure is ≥ 160 mm of Hg and diastolic blood pressure is ≥ 100 mm of Hg[5].

Table – I

JNC 7 Classification of Blood Pressure for Adults ≥ 18 years*

Sl. No.	**Category**	**Systolic BP (mm of Hg)**		**Diastolic BP (mm of Hg)**
1.	Normal	<120	and	<80
2.	Prehypertension	120-139	or	80-89
3.	Hypertension Stage I	140-159	or	90 -99
	Stage II	≥160	or	≥100

* (Source, JAMA 2003; 289:2560)

Prevalence:

Cardiovascular diseases account for a large proportion of all deaths and disability worldwide. In 1990 there were 5.2 million deaths from cardiovascular diseases in economically developed countries and 9.1 million deaths from the same causes in developing countries. In 1990 in India, out of 9.4 million total deaths, cardiovascular diseases caused 2.3 million deaths (25%), 1.2 million deaths were due to coronary heart disease and 0.5 million were due to stroke[6]. It has been predicted that by 2020, there would be a 11.1% increase in cardiovascular deaths in India. Hypertension is a major cardiovascular risk factor and important public health problem in the Indian subcontinent and among the South Asians world-wide[7, 8].

Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths. This fact is important because hypertension is a controllable disease and a 2 mm Hg population-wide decrease in blood pressure can prevent 1,51,000 stroke and 1,53,000 coronary heart disease deaths in India[9, 10].

The average BP levels in China were systolic: 118±18 mm Hg and diastolic: 76.6±11 mm Hg in a sample of 10,076 urban and rural subjects 35-54 years of age. In India Gupta et al reported mean systolic BP (men: rural 127±14, urban 125±17; women: rural 124±13, urban 126±18) and diastolic BP

(men: rural 81±8, urban 81±9; women: rural 80±8, urban 81±12) levels in western Indian urban and rural subjects aged ≥20 years[11]. Systolic BP has increased in Indian men aged 40-49 years from 123±11 mm Hg in 1959 to 128.8±17 mm Hg in 1995[12].

Recent studies among Indians have shown a high prevalence of hypertension in both urban and rural areas[13,14]. The prevalence rate of hypertension in India done by various study groups is shown in the Table – II given in the next page.

Table - II

Recent Indian Hypertension Prevalence Studies (BP >140/90) #

First author	Age group	Place	Sample size		Prevalence (%)	
			Men	Women	Men	Women
Gupta R 1995	20-75	Jaipur	1415	797	29.5	33.5
Joseph A 2000	20-89	Trivandrum	76	130	31	41.2
Anand MP 2000	30-60	Mumbai	1521	141	34.1*	-
Mohan V 2000	20-70	Chennai	518	657	14*	-
Gupta R 2002	20-75	Jaipur	550	573	36.4	37.5
Gupta PC 2004	18-60	Mumbai	40067	59522	43.8	44.5

* Gender specific data not available

(Source, J Human Hypertension 2004; 18: 73-78)

Awareness status of hypertension in India is poor. In urban population of Mumbai there was a very low awareness of hypertension and only 6.1% males and 10.1% females were aware of the hypertension in early 1990`s[15]. In Jaipur also it has been reported that only 11% of male and 16% of female hypertensives were aware of their condition[16]. Higher awareness of hypertension has been reported among the more educated populations in Kerala and among Parsis in Mumbai[17,18]. In community dwelling elderly individuals in Kerala (n= 357, mean age 70 years) hypertension was present in 51.8% subjects and 44.9% of these individuals were aware of their condition[17]. Bharucha and Kuruvilla[18] reported that 53% of men and 44% of women were unaware of their hypertensive status although 905 had their BP measurement in their past. This level of awareness is similar to reported from many developed countries and shows that within India there is a wide variation in hypertension awareness status.

Natural History and Complications:

The pathological hallmark of untreated hypertension is acceleration of atherosclerosis. The higher the BP, the more likely that various cardiovascular diseases will develop prematurely. If untreated, 50% of the hypertensive patients die of coronary artery disease or congestive cardiac failure, about 33% of stroke and 10 – 15% of renal failure. A meta-analysis of nine major

prospective studies shows a direct continuous and apparently independent association of diastolic BP with both coronary artery disease and stroke[19].

In general the vascular complications of hypertension can be considered as either hypertensive or atherosclerotic.

I. Hypertensive Complications:

1. Accelerated malignant phase
2. Hemorrhagic stroke
3. Congestive heart failure
4. Nephrosclerosis
5. Aortic dissection

II. Atherosclerotic Complications:

1. Coronary artery disease
2. Sudden death
3. Arrhythmias
4. Atherothrombotic Stroke
5. Peripheral vascular stroke

Overall Cardiovascular Risk:

The degree of risk from hypertension can be categorized with reasonable accuracy by taking into account

1. The level of Blood Pressure.
2. The biological nature of hypertension based on target organ damage.
3. The co-existence of other cardiovascular risk factors (20).

The goal of anti-hypertensive therapy should not only be the reduction of blood pressure but also treating other risk factors. The major cardiovascular risk factors indicated in JNC-7 report are

1. Hypertension
2. Cigarette smoking
3. Obesity
4. Physical inactivity
5. Dyslipidemia
6. Diabetes mellitus
7. Microalbuminuria or estimated GFR <60 ml/min
8. Age (>55 for men, >65 for women).
9. Family history of premature cardiovascular disease (<55 for men, <65 for women)

Systolic Hypertension and Pulse Pressure:

Systolic blood pressure rises in a linear fashion with age, where as diastolic blood pressure increases until the age of fifty then levels off and even

begins to fall. Isolated diastolic hypertension is more common in younger subjects, while isolated systolic hypertension emerges as the most common form of hypertension in the elderly. The underlying pathological process is loss of arterial elastic tissue, which means that the pressure was created by left ventricular contraction, can no longer be damped by the aorta and major vessels. Systolic blood pressure is a better predictor of cardiovascular risk and isolated systolic hypertension is now recognized to be an independent risk factor of cardiovascular disease. A wide pulse pressure has a similar influence on prognosis[21].

Gender Differences:

Hypertension is an important risk factor for cardiovascular disease in women. Although premenopausal women have lower blood pressure than age matched men, the prevalence of hypertension is higher in women than men after the age of sixty five. Obesity is significantly more common in middle aged and older women and is likely to contribute to cross over in prevalence. Oral contraceptive pills increase the risk of hypertension in younger women. Hormone replacement therapy does not raise the blood pressure in women who are normotensive at the start of treatment.

The ratio of hypertension frequency in women versus men increases from 0.6 to 0.7 at age 30 to 1.1 to 1.2 at age 65 years.

Hypertension in black populations:

Hypertension is most common in black than in white and more common in urban than rural blacks. Black individuals have a higher incidence of salt sensitive hypertension than white individuals and retain more sodium leading to expanded plasma volumes and lower plasma renin activity. The complications of hypertension also tend to be different in blacks with a higher incidence of left ventricular hypertrophy, stroke, renal failure and lower risk of coronary artery disease. The increased frequency of left ventricular hypertrophy and stroke and renal failure is due to severity of hypertension in black and lower risk of coronary artery disease than white is due to more favourable lipid profiles.

Mechanisms of Primary Hypertension:

No single or specific cause is known for most cases of hypertension, and the condition is referred to as primary in preference to essential. Blood pressure is the product of cardiac output and peripheral vascular resistance (BP = CO X PVR). Since persistent hypertension can develop only in response to an increase in cardiac output or a rise in peripheral resistance,

defects may be present in one or more of the multiple factors that affect these two forces. This can be described under the following headings.

1. Non renal factors
2. Renal factors

I. Non renal factors:

Primary hypertension is a complex multifactorial and polygenic disorder that results from an interaction between an individual's genetic background and various environmental factors.

1. Genetic Predisposition:

In studies of twins and family members in which the degree of familial aggregation of blood pressure level is compared with the closeness of genetic sharing, the genetic contributions have been estimated to range from 30% to 60%[22]. Harrap suggested that "the average population blood pressure is determined by the environment but the blood pressure rank within the distribution is decided largely by genes[23].

Epidemiological data suggest that for population variability in blood pressure genetic factors contribute 30 – 35%, common household environment about 10 – 15% and non familial factors for the remaining 50 – 55%[24].

If genetic markers of a predisposition for the development of hypertension are found, then specific environmental manipulations could then be directed toward the susceptible subjects[25]. Pratt, from his observation of bimodal distribution of blood pressure in some families with hypertensive subjects, proposed autosomal dominant mode of inheritance. Pickering proposed that blood pressure is a quantitative trait with genetic contribution which is polygenic.

Genome wide scanning strategy in sib-pairs has identified chromosomal regions on chromosomes 6, 5, 12 and 15 which showed significant linkage to genes that influences inter individual blood pressure variation. There are several candidate genes within the identified group[26].

Polymorphism of genes involving the RAS system, aldosterone synthesis and adrenergic receptors has been noted to be more common in the hypertensive than normotensive patients[27]. Genetic abnormalities may be monogenic in some rare forms of hypertension like glucocorticoid remediable aldosteronism, Liddle syndrome, and apparent mineralocoricoid excess[28].

2. Fetal environment:

Low birth weight as a consequence of fetal under nutrition is followed by an increased incidence of high blood pressure later in life with an overall

estimate that a 1 kg lower birth weight is associated with a 2 to 4 mm Hg higher systolic blood pressure in adulthood[29]. Brenner and Chertow hypothesized that a decreased number of nephrons from the intrauterine growth retardation could very well serve as a permanent irreparable defect that eventuates in hypertension[30].

3. Vascular Remodeling:

A number of factors increase peripheral resistance by both functional contraction and vascular remodeling and hypertrophy. Multiple vasoactive substances act as pressure-growth promoters resulting in both vascular contraction and hypertrophy simultaneously, but perpetuation of hypertension involves hypertrophy. Lever and Harrap[31] postulated that primary hypertension has two mechanisms similar to secondary hypertension (a) a growth promoting process in children, and (b) a self-perpetuating mechanism in adults.

4. Neurohumoral causes of primary hypertension:

A large number of circulatory hormones and locally acting substances may be involved in the development of hypertension which causes hypertension by vascular hypertrophy, capillary rarefaction and impaired microvascular dilation[32].

A. Sympathetic Nervous Hyperactivity:

Young hypertensives tend to have increased levels of circulating catecholamines, augmented sympathetic nerve traffic in muscles, faster heart rate and heightened vascular reactivity to α adrenergic agonists[33].

These changes could raise blood pressure in a number of ways – either alone or in concert with stimulation of renin release by catecholamines or by causing arteriolar and venous constriction or by increasing cardiac output or by altering the normal renal pressure – volume relationship.

B. Renin – Angiotensin System:

Both as a direct pressor and as a growth promoter, the renin – angiotensin mechanism may be also involved in the pathogenesis of hypertension. All functions of renin are mediated through the synthesis of angiotensin II. This system is the primary stimulus for the secretion of aldosterone and hence mediates minerlocorticoid responses to varying sodium intake and volume overload. When sodium intake is reduced or effective plasma volume shrinks the increase in renin – angiotensin II stimulates aldosterone secretion, which in turn is responsible for a portion of the enhanced renal retention of sodium and water.

When large populations of hypertensives are surveyed, only about 30 percent have low plasma renin activity levels, where as 50 percent have normal levels and the remaining 20 percent have high levels[34].

Normal and high renin hypertension:

Some persons with primary hypertension have normal or high renin levels. The concept of "nephron heterogeneity"[35] descried by Sealy and colleagues, assumes a mixture of normal and ischemic nephrons caused by afferent arteriolar narrowing. Excess renin from the ischemic nephrons could raise the total blood renin level to varying degrees and cause high renin levels in patients with primary hypertension.

C. Hyper insulinemia / Insulin resistance:

An association between hypertension and hyperinsulinemia has been recognized for many years, particularly with accompanying obesity but also in about 20 percent of non obese hypertensive patients[36]. The hyperinsulinemia of hypertension arises as a consequence of resistance to the effects of insulin on peripheral glucose utilization. This association does not apply to pima Indians but it has been found in blacks, Asians and as well as whites. The impairment of the peripheral actions of the insulin result from a defect in the usual vasodilatory effect of insulin mediated through increased synthesis of nitric oxide, which normally counters the multiple pressor effects of insulin[37].

These pressor effects include activation of sympathetic activity, a trophic action on vascular hypertrophy, and increased renal sodium reabsorption.

The failure of vasodilation to antagonize the multiple pressor effects of insulin presumably eventuates in a rise in blood pressure that may be either a primary cause of hypertension or, at least, a secondary potentiator.

D. Endothelial Cell dysfunction:

The endothelium is now known to be the source of multiple relaxing and contracting substances, of which nitric oxide is an important vasodilator[38]. The impairment of normal vasodilation in the insulin resistance syndrome has been shown to involve failure to synthesize the normal endothelium derived relaxing factor (NO).

Nitric Oxide:

Hypertensive patients have been shown to have a reduced vasodilatory response to various stimuli of nitric oxide release that appears to be independent of the etiology of the hypertension and the degree of the gross vascular structural alteration. Impaired nitric oxide mediated vasodilation may promote abnormal vascular remodeling and may be involved in the greater propensity for vascular damage in blacks than in whites. Nitric oxide –

mediated forearm responsiveness has been restored by normalization of blood pressure by anti hypertensive drugs with different modes of action.

Endothelin:

Endothelin – 1 causes pronounced and prolonged vasoconstriction and because blockade of its receptors improves endothelium – dependent vasodilation in hypertensive patients[39].

E. Minerals:

Excess of lead and changing ratios among dietary sodium, potassium, calcium and magnesium have also been postulated in the pathogenesis of primary hypertension[40].

II. Renal retention of excess dietary sodium:

A considerable amount of circumstantial evidence supports a role for sodium in the genesis of hypertension. To induce hypertension, some of the excess sodium must be retained by the kidneys. Such retention could arise in a number of ways.

1. Nephron heterogeneity, described as the presence of a sub population of nephrons that is ischemic either from afferent arteriolar vasoconstriction or from an intrinsic narrowing of the lumen. Renin secretion from this sub group of nephrons is tonically elevated. This

increased renin secretion then interferes with the compensatory capacity of intermingled normal nephrons to adaptively excrete sodium and consequently, over all blood pressure homeostasis[35].

2. A decrease in the filtration surface by a congenital or acquired deficiency in nephron number or function.
3. A resetting of the normal pressure – natriuresis relationship – the Guyton hypothesis[41].
4. An acquired inhibitor of the sodium pump or other abnormalities in sodium transport[42].
5. Defensive responsiveness to atrial natriuretic hormones[43].

Association of hypertension with other conditions:

1. **Physical inactivity:**

Physical fitness may help prevent hypertension and persons who are already hypertensive may lower their blood pressure by means of regular isotonic exercise. The relation ship may involve insulin resistance because an increased resistance was coupled with low physical fitness in normotensive men with a family history of hypertension.

2. **Alcohol:**

Alcohol in larger amounts (more than two portions a day and more so when drunk in binges) increases blood pressure and arterial stiffness. The

pressure effect of larger amount of alcohol reflects an increase in cardiac output and heart rate, possibly a consequence of increased sympathetic nerve activity. Alcohol also alters cell membranes and allows more calcium to enter, perhaps by inhibition of sodium transport.

Alcohol in small amounts (less than one or two usual portions a day) provides protection from coronary disease, congestive heart failure, stroke, and dementia[44]. And at least in women, reduces the incidence of hypertension[45]. The reduction in coronary disease in persons who ingest small amounts of alcohol may reflect an improvement in lipid profile, a reduction in factors that encourage thrombosis, and an improvement in insulin sensitivity.

Framingham study showed small overall correlation between alcohol intake and blood pressure, but prevalence of hypertension was about two times higher among persons drinking sixty ounce or more of ethyl alcohol per month than among those drinking less than thirty ounce per month[46].

3. Smoking:

Cigarette smoking raises blood pressure, probably through the nicotine induced release of norepinephrine from adrenergic nerve endings. In addition, smoking causes an acute and marked reduction in radial artery compliance independent of the increase in blood pressure. When smokers quit, a rise in the blood pressure may occur, probably reflecting a gain in weight. Numerous

studies have shown that smokers are thinner than non smokers and that smoking reduces weight. However they will have larger waist hip ratio than non smokers[47].

4. **Hematological Findings:**

Higher hematocrits are found in hypertensive persons and are associated with abnormal left ventricular filling on echocardiography[48]. Whole blood viscosity in increased by about 10 percent in persons with untreated mild hypertension, comparable to the increase in their peripheral resistance[49]. Pseudo or stress polycythemia with high hematocrit and increased blood viscosity but contracted plasma volume, as well as normal red cell mass and serum erythropoietin levels are found in hypertension. High WBC count is predictive of the hypertension[50].

5. **Hyperuricemia:**

Hyperuricemia is present in 25 percent of individuals with untreated hypertension, more than 75% of patients with malignant hypertension which are about five times the frequency found in normotensive persons[51]. Hyperuricemia probably reflects decreased renal blood flow, presumably a reflection of nephrosclerosis.

6. **Sleep Apnea:**

Snoring and sleep apnea are often associated with hypertension, which may in turn be induced by the increased sympathetic activity and endothelin release in response to hypoxemia during apnea[52].

7. **Hypercholesterolemia:**

Hypercholesterolemia frequently coexists with hypertension, at least in part because it impairs endothelium – dependent vasodialtion. Lipid lowering therapy restores the bioavailability of nitric oxide, reduces arterial stiffness, and lowers blood pressure[53].

8. **Obesity:**

The majority of patients with high blood pressure are overweight and hypertension is about six times more common than it is in lean subjects[54].

A 10 kg higher body weight is associated with a 3 mm Hg higher systolic and 2.3 mm Hg higher diastolic blood pressure. These increases translate into an estimated 12% increase in the risk of coronary artery disease and 2.24% increase in the risk of stroke.

Body mass index in widely used as a correlation with excess body fat or adiposity but it does not convey information on required fat distribution. Body fat distribution plays a role as a risk factor for hypertension. An increase

in waist hip ratio (WHR) > 0.95 in male and 0.8 in female is an independent risk factor for the development of hypertension and is independently associated with hypertriglyceride and increased apoprotein – B. The waist circumference may be the better indicator of visceral fat than waist hip ratio.

Hip circumference – It is measured at the point of one third of the distance between the anterior superior iliac spine and the patella.

Waist Circumference – It is measured half way between superior iliac crest and rib cage in mid axillary line. It correlates well with the systolic blood pressure and diabetes mellitus.

Body mass index = weight in kg / height in m^2.

Table - III

Proposed classification of weight by BMI in adult Asians (55) *

Classification	BMI (kg / m^2)
Underweight	<18.5
Normal range	18.5 – 22.9
Over weight	23
At risk	23 – 24.9
Obese I	25 – 29
Obese II	>30

* (Source, Am J Clin Nutr. 2000; 72: 1067-1068)

Metabolic syndrome:

According to ATP III, metabolic syndrome is defined as a cluster of cardiovascular risks in a silver individual – normally hypertension, diabetes mellitus, abdominal obesity, low HDL, increased TGL, procoagulant tendency and increased small LDL.

Obese individuals with high waist hip ratio have high incidence of hypertension than do with low waist hip ratio[56]. Visceral obesity is a strong risk factor for hypertension. Although body mass index is a very strong determinant of blood pressure, a visceral distribution of fat has an even greater relationship with the development of hypertension[57].

CALCIUM

Calcium is an important mineral mainly found in bone and teeth.

Dietary sources

It is widely distributed in food sub such as milk, cheese, egg-yolk, beans, lentils, nuts, figs, cabbage.

Body distribution

The total calcium of the body is 25-35 males (100g-170g) about 99% and it is found in bones. It exists as carbonate on phosphate and calcium. About 0.5% in soft tissue and 0.1% in ECF. The normal level and plasma calcium is 9-11mg/dl. The calcium in plasma in and 3 types, namely,

- Ionized calcium (diffusible)
- Protein bound ca++
- Complex ca++

About 40% and total calcium is in ionized form albumin is the major protein with which calcium is bound. All the three forms and cal+ in plasma remain in equilibrium with each other. Ionized calcium in physiologically admit form and calcium[58].

CALCIUM IN THE PATHOGENESIS OF ESSENTIAL HYPERTENSION:

Essential hypertension is accompanied by abnormalities of calcium homeostasis, including hyperparathyroidism with reduced target organ responses to parathyroid harmone in kidney and bone. Hyperparathyroidism is also due to an intrinsic defect in renal calcium handling. In subject with a genetically determined predisposition to the development of hypertension, a high sodium consumption leads to volume overload, which results in the appearance of a natriuretic hormone in the circulation[87]. It has been suggested that the excessive excretion of calcium and phosphorous associated with exaggerated natriuresis may participate in aberration of calcium metabolism in low rennin hypertensive seniles.

By definition, natriuretic hormone causes natriuresis by blocking sodium reabsoption in the renal tubles and this blockade appears to involve inhibition of the ouabain sensitive Na-K pump that activity extrudes sodium into the extracellular fluid.

This natriuretic hormone influences membrane permeability which leads to an increase in intracellular sodium and by inhibiting sodium calcium exchange, causes an accumulation of calcium in vascular smooth muscle cells. The increase in intracellular calcium then leads to an increased contractility and vascular tone resulting in an augmented peripheral vascular tone resulting in an augmented peripheral vascular resistance and consequently in raised blood pressure[87].

Increased intracellular sodium will raise the concentration of free calcium within the vascular smooth muscle cells. A number of relations exists between sodium and calcium that would explain how this happens.

Blaustein portrays some of these[59]:

1. An inhibition of sodium potassium exchange pumps would depolarize the muscle fibre and thereby increase calcium entry through voltage – sensitive calcium channels.
2. An increase in intracellular sodium will result in a smaller sodium (Na) electrochemical gradient between the sarcoplasm and external medium,

thereby decreasing the extrusion of calcium from the cell via the Na-Ca exchange which derives its energy from this gradient.

3. An increase in intracellular sodium in the presynaptic terminals of sympathetic neurons promotes calcium dependent norepinephrine release. The norepinephrine releases calcium from intracellular stores.

However, the higher intracellular sodium acts to increase the concentration of intracellular calcium, a very small rise in intracellular sodium, can by theoretical calculations, be shown to cause enough of a rise in intracellular calcium to increase the resting tone of vascular smooth muscle by about 50%.

Other mechanisms may be responsible for higher intracellular calcium in hypertension:

1. The inner side of RBC members from hypertensive patients.
2. Passive calcium influx was increased,
3. ATP-dependent calcium extrusion is reduced in red cells from SHR rate.

In summary, vascular smooth muscle intracellular calcium is likely elevated in primary hypertension. Since intracellular calcium directly controls vascular contraction and relaxation, the connection to hypertension in obvious. Increased vascular tone and reactivity are likely responsible for much of the

increased total peripheral vascular resistance that is the primary cause of sustained hypertension.

The significance of the reduced binding of calcium to the inner aspect of the plasma membrane is not clear. Calcium exerts an important regulatory effect on various aspects of membrane function and it is possible that the reduction in binding is a cause of some of the abnormalities of ion transport. It may be, however, that the reduction in binding is merely a marker of an alteration in membrane composition. Which results in a reduced availability of binding sites.

RELATION BETWEEN WHOLE BODY CALCIUM METABOLISH AND EVENTS AT A CELLULAR LEVEL:

Evidences suggest some mechanism by which the calcium balance of the body as a whole can influence events at a cellular level. The link may involve change in the plasma ionized calcium concentration or changes in calcium regulating substances such as parathyroid hormone or 1-25 dihydroxy vitamin D. A rising concentration of calcium in the extracellular fluid has been shown to inactivate certain potential operated calcium channels in tenia coil and a falling concentration must have contrary effects. It is probable that human resistance vessels respond in a similar way, although the manifest response to a rise in calcium concentration is contraction. Parathyroid hormone probably acts on cell of many types apart from those of renal tubules

and bone, and increase in cytosolic calcium. At concentration, greatly in excess of those occurring physiologically. Parathyroid hormone dilates resistance vessels, but the effect, if any, of the very small increases observed in patients with primary hypertension is unknown. It is possible that a mechanism exists by which the free calcium in the intake, but it seems likely that the disorder of calcium handling at a cellular level predominantly from other causes[60].

Effect of alteration in calcium intake. If a calcium intake that is suboptimal relative to need plays any part in the causation of primary hypertension, it would be expected that the administration of calcium supplements would lower blood pressure, at least in the early stages of the hypertensive process. In rats, the administration of large doses of calcium supplements ameliorates the hypertensive process and severe calcium deprivation aggravates it. In a well designed and well controlled study, the effect of 8 weeks of treatment with a calcium supplement (calcium carbonate, 25 mmol/day) in 32 normal subjects and 48 patients with mild hypertension was observed. In the normal subjects there was little effect, with no more than a small but statistically significant fall in supine diastolic pressure. In the patients treatment with calcium led after 8 weeks to significant fall in supine diastolic pressure, in the supine position and both systolic and diastolic pressure on standing position. In another limited placebo-controlled and

randomized study, 8 subjects with mild to moderate hypertension were given 20 mmol calcium daily as sandocal for 8 week periods: mean arterial blood pressure fell by less than 1mm of Hg despite a significant increase in urinary calcium excretion.

Altered calcium metabolism plays a more important role in hypertension developing during pregnancy. An increase in platelet calcium and RBC sodium have been found in these patients and has been given much importance in the initiation and maintenance of hypertension and influencing peripheral vascular resistance and also various other factors in the serum of PIH (pregnancy induced hypertension) women and these may contribute to the accumulation of intracellular ionized calcium in patients with pregnancy(25 and 50mmol/day) there is a significant reduction in diastolic blood pressure during the second trimester and with the larger supplement, the normal increases in pressure in the third trimester can be prevented [61].

It is of interest that Yamakawa et al [62] have shown that disturbed intraplatelet and systemic calcium metabolism may be of predictive value in the development of hypertension.

AIMS AND OBJECTIVES

1. To study the levels of serum calcium in patients with primary hypertension.

2. To correlate the serum calcium levels with blood pressure.

MATERIALS AND METHODS

Setting : The work was carried out in the outpatient department and medical wards of Govt. Rajaji Hospital, Madurai.

Design of the study : Analytical study

Period of the Study : One year – February 2005 to January 2006

Sample size : 100 cases (70 cases and 30 controls)

Ethical committee approval : The present project was approved by the ethical committee.

Inclusion criteria:

1. Patients with primary hypertension.
2. Patients whose age was above 18 years were included.
3. Both sexes were included.

Exclusion Criteria:

1. Patients below 18 years.
2. Patients with renal failure.
3. Pregnancy.
4. Patients with secondary hypertension.
5. Patients on non-steroidal anti-inflammatory agents, antihypertensives, diuretics, beta blockers or stimulants.
6. Patients with malignant hypertension.

7. Females on oral contraceptive medication.
8. Patients with peripheral vascular disease.
9. Patients with diabetes mellitus.
10. Patients with acute diarrhoeal diseases.

Consent:

The study group thus identified by the above criteria (inclusion and exclusion criteria) was first instructed about the nature of the study. Willing participants were taken up after getting a written informed consent from them.

Study Subjects and Controls:

Seventy newly diagnosed essential hypertensive patients attending the medicine OPD or admitted to the medical wards of Govt. Rajaji Hospital for the period of one year from February 2005 to January 2006 formed the study group. Thirty healthy people were kept as controls. This control group comprised of normotensive individuals who were attendants of patients with primary hypertension living in the same environment other than their own siblings.

Details of the Study Subjects:

All the patients were subjected to detailed history taking, careful physical examination and biochemical analysis to exclude secondary hypertension.

Patient's height and weight were measured. The body mass index was calculated using the formula weight / height ^{2}. Patient's hip and waist circumferences were measured. All the peripheral pulses were checked with special attention to carotid and the femoral to detect evidence for early atherosclerosis. An ocular fundus examination was done to detect hypertensive retinopathy.

Patients were informed to refrain from smoking or drinking tea or coffee for at least thirty minutes before measuring blood pressure. Then blood pressure was measured using the following guidelines.

Guidelines for measuring blood pressure:

I CONDITIONS FOR THE PATIENT

A. Posture:

1. Sitting postures are usually adequate for routine follow-up. Patient should sit quietly with back supported for five minutes and arm supported at the level of heart.

2. For patients who are over 65, diabetic or receiving anti-hypertensive therapy, check for postural changes by taking readings immediately and 2 minutes after the patient stands.

B. Circumstances:

1. No caffeine for preceding hour
2. No smoking for preceding 15 minutes.
3. No exogenous adrenergic stimulants like phenylephrine in nasal decongestants or eye drops for papillary dilation.
4. A quite, warm setting.
5. Home readings taken under various circumstances and 24 hour ambulatory recordings may be preferable.

II EQUIPMENT:

A. Cuff Size:

The bladder should encircle and cover 2/3rds of the arm length. If not, place the bladder over the brachial artery; if bladder is small spuriously high readings may result.

B. Manometer:

1. Aneroid gauges should be calibrated every six months against the mercury manometer.

2. For infants use ultrasound equipment e.g., the Doppler method.

III TECHNIQUE:

A. Number of readings:

1. On each occasion, take at least two readings, separated by as much time as practical. If readings vary by more than 5 mm Hg, take additional readings until two are close.
2. For diagnosis, obtain at least three sets of readings a week apart.
3. Initially, take pressure in both arms, if pressure differs, use arm with higher pressure.
4. If arm pressure is elevated, take pressure in one leg, particularly in patients below age 30.

B. Performance:

1. Inflate the bladder quickly to a pressure 20 mm Hg above the systolic, as recognized by the disappearance of the radial pulse.
2. Deflate the bladder 3 mm Hg every second.
3. Record the Korotkoff phase V (disappearance) except in children, in whom use of phase IV (muffling) is advocated.
4. If Korotkoff sounds are weak, have the patients raise the arm, open and close the hand 5 to 10 times, after which the bladder should be inflated quickly.

C. Recording:

Note the pressure, patient position, the arm, cuff size (e.g., 140/90, seated, right arm, large adult cuff).

Urine albumin, sugar, microscopy and pH were done for all the subjects. A twelve lead electrocardiogram and chest x ray were also taken.

Overnight (12 hour) fasting blood sugar and urea was done by using Diacetyl monoxime (DAM) technique. Serum creatinine was estimated using COBAS auto analyzer. Serum Calcium was estimated using Cresolphthalein complexone method, total protein was estimated by biuret method and albumin was estimated by BCG method.

DEFINITIONS USED IN THE PRESENT STUDY:

Essential Hypertension:

Hypertension was defined in accordance to the JNC- VII report as systolic blood pressure 140 mm of Hg and above and or diastolic blood pressure 90 mm of Hg and above. The diagnosis that the hypertension is essential and not secondary was made on the overall clinical impression only. Laboratory investigations to rule out secondary causes were not done in each case.

Calcium Normal Values:

The normal range for serum calcium is from 9 to 11 mg/dl.

Obesity:

According to the proposed classification of weight by BMI in adult Asians (55), the patients with a BMI <18.5 were classified as underweight, 1.85 – 22.9 were classified as normal, ≥ 23 were classified as overweight and ≥ 25 were classified as obese.

Diabetes Mellitus:

Patients with fasting plasma glucose ≥ 126 mg / dl or two hour plasma glucose ≥ 200 mg / dl or with symptoms of diabetes plus random blood glucose ≥ 200 mg / dl were considered to be diabetic.

Left ventricular hypertrophy:

Based on the electrocardiographic findings, which satisfy either Sokolow-Lyton criteria or Cornell voltage criteria [63,64].

Conflict of interest:

There was no conflict of interest.

Financial Support:

Nil.

Limitations:

1. Only serum calcium alone done.
2. Twenty four hours urinary calcium and arterial blood gas analysis were not done due to technical and financial limitations.

Renal handling of calcium was not attempted as it was beyond the scope of the present study.

3. Hormones related to calcium handling was not estimated.
4. Serum ionized calcium level was not measured.

Statistical Analysis:

The collected data was entered in Microsoft excel spread sheet and analysed statistically using epidemiological Information package – 2002 developed by centers for disease control and prevention, Atlanta in collaboration with World Health Organization. Student 't' values were applied for significance. Significance was considered if the 'p' value was below 0.05.

't' test is used to find out whether or not there exist a mean difference between the two groups. If there is then it attempts to see whether or not there exist a statistical significant differences between the means of the two groups.

$$t = \frac{\overline{X1} - \overline{X2}}{\sqrt{\frac{SD_1^2}{n1} + \frac{SD_2^2}{n2}}} \quad \text{with } (n1+n2-2) \text{ as df}$$

$\overline{X1}, \overline{X2}$ = means of two groups

SD1, SD2 are standard deviation of two groups

n1, n2 are the sample size

RESULTS AND OBSERVATIONS

The total number of subjects included in this study was 100. Among these 100 subjects, 70 were cases (Hypertensive) and 30 were controls (Normotensive).

Analysis of cases and controls with respect to age:

The age of the subjects in the study group ranged from forty to sixty years. The mean and standard deviation for the age of the cases and controls were 53.1 ± 5.37 years and 51.5 ± 5.38 years respectively. The study group and the control group did not differ from each other statistically with reference to age.

Majority of the patients in both the study and control group lie between 41 and 60 years. There was no significant difference in the age composition of those with and without hypertension in this study. Almost same age group of patients was selected in both groups.

The distribution of the cases and controls in relation to age is provided in the Table – IV given below.

Table – IV

Distribution of cases and controls in relation to age

Age group	Cases		Controls	
	No	%	No	%
41 – 50	24	34.3	18	60
51 – 60	46	65.7	12	40
Total	70	100	30	100
Mean	53.1		51.5	
S.D	5.37		5.38	

The mean age distribution for the males in the case and control groups was 52.92 ± 5.52 years and 50.28 ± 5.66 years respectively. The mean age distribution for the females in the case and control groups was 53.31 ± 5.27 years and 51.8 ± 2.17 years respectively.

Gender:

Among the 70 cases studied, there were 38 males and 32 females. Among the 30 controls, there were 20 males and 10 females.

The details are given in the Table – V provided below.

Table – V

Distribution of cases and controls in relation to gender

Sex	Cases		Controls	
	No	**%**	**No**	**%**
Male	38	54.3	20	66.7
Female	32	45.7	10	33.3
Total	70	100	30	100

Analysis of cases and controls with respect to Body Mass Index (BMI)

34.3% of cases were obese while in the control group obesity was noticed in 3.3%. The details are shown in the Table – VI given below.

Table – VI

Distribution of cases and controls with respect to Body Mass Index (BMI)

BMI	Cases		Controls	
	No	%	No	%
Underweight <18.5	7	10	3	10
Normal weight 18.5 – 22.9	24	34.3	20	66.7
Overweight 23 – 24.9	15	21.4	6	20
Obese > 25	24	34.3	1	3.3
Total	70	100	30	100

The mean body mass index in the case group is 23.73 ± 3.28 and in the control group is 21.36 ± 2.12. The details are given in the Table – VII given below.

Table – VII

BMI among cases and controls

BMI	Cases	Controls
Mean	23.78	21.36
S.D.	3.28	2.12

'p' value = 0.00004

This shows that the difference in Body Mass Index between cases and controls was statistically significant.

The mean BMI of cases and controls according to gender is given in the Table – VIII below.

Table – VIII

BMI of cases and controls with respect to gender

Group	Male		Female	
	Mean	**S.D.**	**Mean**	**S.D**
Cases	23.78	3.49	23.68	3.07
Controls	20.9	1.62	23.62	2.21

The mean body mass index in male (case group) is 23.78 and control 20.9, in female case 23.68 and control 23.62. The details are given in the Table VIII.

BMI in relation to the grading of hypertension is furnished in the Table– IX given below.

Table – IX

BMI with respect to Hypertension

BMI	Grade I Hypertension		Grade II Hypertension	
	No.	%	No.	%
Underweight <18.5	-	-	6	8.6
Normal 18.6 – 22.9	5	7.1	20	28.6
Overweight 23 – 24.9	4	5.7	11	15.7
Obese >25	2	2.9	22	31.4

Body mass index was independent of gender and electrolyte status, but it was significantly more in those with grade II hypertension.

Analysis of cases with respect to presenting symptoms

The most common presenting symptom is giddiness. The other symptoms were in the order of headache, chest pain, palpitation and dyspnoea. The details of the presenting symptoms are given in the Table – X given below.

Table – X

Analysis of presenting symptoms

Symptoms	Male		Female	
	No.	%	No.	%
Nil	1	1.4	1	1.4
Headache	7	10	1	1.4
Giddiness	18	25.7	19	27.1
Chest pain	6	8.6	3	4.3
Palpitation	4	5.7	8	11.4
Dyspnoea	2	2.9	-	-

History of headache and chest pain was noticed among men and these patients were suffering from very high blood pressure. In contrast history of palpitation was elicited more among women.

Distribution of cases and controls with respect to cardio vascular risk factors

Analysis of other risk factors like smoking, alcoholism and family history were done among hypertensives. Their details are furnished in the Table – XI below.

Table – XI

Risk factors among cases and controls

	Smoking		**Alcohol**		**Both**	**Family history**	
	Yes	**No**	**Yes**	**No**		**Yes**	**No**
Cases	27	43	10	60	8	10	60
Control	14	16	6	24	8	-	30

Since alcoholism and smoking were noticed among men only in this part of the country, statistical analysis was not attempted for these risk factors.

Blood pressure distribution among cases

The details of the blood pressure distribution are given in the Table – XII given below.

Table – XII

Distribution of systolic and diastolic blood pressure

Blood Pressure	Cases	Control
	Mean + SD	Mean + SD
Systolic	172.14 ± 15.12	106.53 ± 6.37
Diastolic	103.29 ± 6.07	71.4 ± 4.24

The mean systolic blood pressure for the cases was 172.14 ± 15.12 mm Hg. Similarly the mean diastolic blood pressure for the cases was 103.29 ± 6.07 mm Hg. Since the systolic and diastolic blood pressure was elevated in cases and it was due to the nature of the disease taken into study, the statistical analysis was not done.

The mean systolic and diastolic blood pressure distribution for the males was 172.63 ± 16.71 mm Hg and 103.42 ± 7.08 mm Hg respectively. Similarly for the females the mean systolic and diastolic blood pressure distribution was 171.56 ± 13.22 mm Hg and 103.13 ± 4.71 mm Hg respectively. There was no statistical significance in the systolic and diastolic blood pressure among the cases.

The distribution of cases with respect to grading of hypertension is given in the Table – XIII given below.

Table – XIII

Distribution of cases with respect to grading of hypertension

Subject	Grade I		Grade II	
	No	%	No	%
Cases	11	15.7	59	84.3

From our statistical analysis patients with Grade II hypertension were significantly higher than Grade I hypertension.

Distribution of cases and controls in relation to serum calcium

Serum calcium in the study population varied from 6.9mg/dl to 10.9mg/dl. The man and standard deviation and serum calcium among cases was 8.87±1.07 mg/dl while in control group it was 9.66±0.61mg/dl respectively.

This table clearly shows that the serum calcium level was significantly lower among hypertension population studied.

The details are given in Table XIV

	Case		**Control**		**t value**	**'p' value**
	Mean	**SD**	**Mean**	**SD**		
Serum calcium	70 8.87	1.071	30 9.66	0.617	4.62	$p<0.05$

Serum calcium in relation to systolic BP

The mean value of serum calcium was 8.90 in Grade I systolic BP and 8.85 in Grade II systolic BP among cases.

The mean value of serum calcium was 9.66 among controls. This is shown in table XV given below. This table clearly shows that the serum ca++ level was significantly lower among Grade II systolic BP cases studied.

The details are given in Table XV

Systolic BP	Mean	S.D	t value	'p' value
Grade I	8.90	1.082	0.18	$p<0.05$
Grade II	8.85	1.076		

Serum calcium in relation to diastolic BP

The mean value serum calcium was 9.20 in mg/dl Grade I systolic BP of 8.86 in Grade II diastolic BP among cases. The mean value of serum calcium was 9.66 among controls. This is shown in Table XVI given below. This Table clearly that the serum calcium level was significantly lower among Grade II diastolic BP cases studied.

The details are given in Table XVI

Diastolic BP	Mean	S.D	t value	'p' value
Grade I	9.20	0.70	0.65	$p<0.05$
Grade II	8.86	1.08		

Serum Calcium in relation to age

Serum calcium in the study population varied from 6.9mg/dl to 10.9 mg/dl. Correlation between age (case and control) and serum calcium is – 0.1863 i.e., KARL PEARSON'S r = -0.1863. It shows that negative correlation between age and serum calcium but non significant. Correlation between age in systemic hypertension and serum calcium is -0.1157 i.e., higher the age less the serum calcium but this value is not significant. KARL PEARSON'S r = -0.1157.

Correlation between sex and serum calcium

For total population

The details are given in Table XVII

Sex	N	Mean	S.D	' t 'value	'P' value
Male	60	9.211	1.02	1.24	P> 0.05
Female	40	8.955	1.01		not significant

Sr. calcium in the total population varied from 6.9ms/dl to 10.9ms/dl. The mean & S.D of Sr. calcium among male was 9.21 ± 1.02 while in female it was 8.95 ± 1.02 while in female it was 8.95 ± 1.01 respectively.

For SHT Patients group

The details are given in Table XVIII

Group	N	Mean	S.D	't' Value	"p" value
Male	40	8.99	1.11	1.10	P > 0.05
Female	30	8.71	1.01		(N.S)

In SHT patients, the mean and SD of serum calcium among male was 8.99 ms/ dl ± 1.11 in female systemic hypertension patient (40) was 8.71 ± 1.01 buts 'p' value in not significant.

For control group:

The details are given in Table XIX

Group	N	Mean	S.D	't' Value	"p" value
Male	40	9.65	0.631	-0.12	P > 0.05 (N.S)
Female	10	9.68	0.620		

The mean and SD of serum calcium among male was 9.65 ± 0.63 and in female control serum (10) was 9.68 ± 0.620. This table clearly show that serum calcium level in negative correlation but not significant.

Correlation = -0.0287

Areas for further research

1. To identify the markers of hypertension prone population.

2. To find out the genes responsible for calcium handling and if required to develop a biomolecule to overcome the effects of the mediators of which signal / control the calcium at the molecular level.

DISCUSSION

Hypertension is one of the leading causes of death and disability among all over the world. Hypertension the most common form and cardiovascular disease is present nearly 25% of adults and increases in prevalence with age. It remains the major risk factor for coronary, central and peripheral vascular disease. Essential hypertension comprises more than 90% of hypertension[1].

Patients were studied on the basis of clinical parameters and simple biochemical investigations serum calcium and albumin was done for all the patients.

In our study the mean serum calcium was estimated in the control and study groups. Results were compared with other studies.

Serum calcium was lower in the hypertensive group than the control group eventhough both were with in normal range. The mean and standard deviation of serum calcium among cases was 8.87±1.07mg/dl while in control group if was 9.66±0.61mg/dl respectively.

Our study was supported by P.P.Readdy et al (2004), O Stmania University, Resumpet, Hyderabad. In his study serum calcium levels were measured in 117 subjects with E.T. and 77 first degree relatives. The results showed that serum calcium levels the significantly ($p<0.01$) decreased in both males: females with essential hypertension and their first degree relatives

when compared with the normotensive controls. This is the first study in Indian population[63].

In Tromso study conducted in northern Norway, U large health surveys have been performed the first 1974 of last in 1994-1995. Total serum calcium levels were measured in 12865 men and 14293 women between ages and 25 and 97 years. With the use of sex specific multiple linear regression model with age calcium and body mass index cholesterol, HDL, triglycerides, systolic and diastolic blood pressure and pulse as possible covariates, serum calcium was significantly ($p<0.001$) and positively association with systolic and diastolic blood pressure, serum cholesterol and HDL cholesterol in both sexes.

In Tillman DM and Semple PF study shows that disturbance of calcium metabolism have been described in hypertension, measurement of plasma and serum concentration of ionized calcium, total calcium, magnesium and serum were made in 38 patients with E.T. and age and sex-matched control subjects. Urinary excretion of calcium, magnesium and sodium was also determined. The mean serum concentration and ionized calcium was 1.23±0.04 (SD) mmol/l in HT group and 1.21±0.03mmol/l in control and results were similar after correction for pH. There was a weak positive correlation between serum ionized calcium pH 7.4 and systolic pressure ($r=0.26$, p less than 0.02) but no correlation with plasma renin concentration. Although the difference between

serum total calcium concentration in the hypertensive (2.29±0.09mmol/l) and control (2.26±0.01mmol/l) subject was not significant, there was significant correlation between total calcium and systolic pressure ($r=0.23$, $p<0.05$) which was maintained after correction for other variables[64].

In Touyz RH et al study conducted in Johannesburg, South Africa, states that the heterogeneous status of magnesium and calcium metabolism in hypertensive population may be related to the plasma renin activity (PRA). 39 normotensive (20 black, 19white) and 47 hypertensive (2 black, 22 white) subjects were studied. PRA and ionized calcium were significantly lower in black hypertensive as compared with the white hypertensive group (1.99±0.3 vs 5.6±1.02ng) ml/h for RA; 1.28±0.07 vs 1.42±0.01mmol/l for ionized calcium : black hypertensives as compared with white hypertensives group ($p<0.05$). Ionized calcium was significantly increased ($p<0.05$) in white hypertensive patient as compared with the normotensive control (1.42±0.01 vs 1.29±0.04 mmol/l)[65].

In shone AC study states that serum ionized calcium and pH : effects of blood storage, some physiological, influences of a comparison between normotensive and hypertension subjects. We proceeded to examine a group of age, sex and race matched hypertension and normotensive subjective under standardized conditions designed to minimize such technical and physiological artifacts. Ionized calcium was not significantly different in the

two groups. However, serum pH was significantly elevated in the hypertensive group. In the combined group of normotensive and hypertension subjects, serum pH was significantly correlated with blood pressure[66].

In Lind L study states that a pattern of negative calcium balanced with lowered levels of serum ionized calcium (ca^{2+}) increased urinary excretion of calcium has been reported in hypertensive men. In a present study 10 untreated hypertensive subjects were salt loaded (20 gram Nacl) for one week after a weak on a low salt diet (3g). The change in mean blood pressure at the end of the high compared with the low salt diet was called salt sensitivity and was related to index of mineral metabolism. It was found that salt sensitivity and was related to indexes of mineral metabolism. It was found that salt sensitivity was significantly correlated with both plasma ionized ca+ and serum calcium concentration both $r=0.64$, $p<0.05$ on different diet. Salt loading increased the urinary excreation and calcium by 95% and also induced reduction in Hb, serum albumin and serum calcium ($p<0.0001$). In conclusion, low levels and plasma ionized calcium and serum calcium where mainly support in hypertensive subjects with a low sensitivity to salt. The findings support the view that calcium metabolism in related to the regulation of BP[67].

SUPPLEMENTATION OF CALCIUM OF ITS RESPONSE IN VARIOUS STUDIES

Location & population	Sample size age	Pt conditions & study design	Ca+ dose duration	Results
Guatemala 1983[68]	N=57 Age 18-35	S/P	1g/ 22 weeks	↓ in HT no change in NTN
Oregon 1985[69]	n=48 HTN n=32 (N) Age 21-70	NTN/HTN / cross over	1g/ 8 weeks	↓ in HT: no change in NTN
England 1986[70]	n=8 Age 20-43	NTN/CR	1.8g/ controlled diet 1 week	No change
Netherlands 1986[71]	n=90 Age 16-29	Double blind	1g/ 12 weeks	↓ in DBP
Australia 1986[72]	n=47 HTN n-48 NTN Mean age Placebo 60±3 10mmol 53±5 20mmol 59±3	NTN / HTN / S/P	10mmol-20mmol/2mths	No change
Italy 1986[73]	n=18 Mean age 43±9	Mild HTN S/P D-B: CR	1gm/15 weeks	↓ in standing SBP
Japan 1986[74]	n=14 Mean age 71 (ca^2+) 73 (ca^2+d3)	HTN	2gca^2+/ 2gca^2++D_3/ 8 weeks	↓ sys BP ca2+ no change in ca2+ D3
Indiana 1987[75]	n=75 men Age 19-52 yrs	NTN S/P	1.5g/ 12weeks	↓ SBP ↓ DBP
South Dakota 1987[76]	n=24 women Mean age 57±9.5	Mild HT	1g / 12 weeks	↓ in SBP
Greece 1987[77]	n=18 Age 25-60	Mild / mod HT S/P: CR	1gm/ 5 days	↓ in SBP

Location & population	Sample size age	Pt conditions & study design	Ca+ dose duration	Results
England 1987[78]	n=18 Age 28-65	Mild /mot HT/S/P/CR : D-B	1.6gm/1 month	No change
Italy 1987[79]	n=8 Mean age 40±3	Mild HTN S/P: D-B:CR	1gm/ 3weeks	No change
California 1991[80]	n=19 Age 30-65	Mild HTN D-B:CR	1.2gm/3mths	No change
Japan 1991[81]	n=9 Age 65-86	HTN CR	1gm/8 weeks	↓ed in mean pressure
Oregon 1992[82]	n=103 Age 50-80	HTN D-B	1gm/ 12/42 weeks	No mean difference @ 12 weeks
Indiana 1992[83]	n=42 Mean age: placebo 35.9±15.7 Rx32.3±10.7	HTN D-B	1.5gm 8 weeks	↓ in mean pressure
US Multicenter 1992 (TOHP)[84]	n=237ca2+ n=237 placebo Age 30-54	S/P D-B	1/6mths	No change

HTN - Hypertension NTN - Normotinsive
S/P - Supplement / Placeto D-B - Double blind
CR - Cross Over

With respect to blood pressure, the clinical trial findings when calcium intake is increased are conflicting, but there is a trend toward a positive effect with calcium supplements of 1.0 to 1.55 per day. The findings have been highly variable across studies and within studies but the largest study (TOHP) - Trials and Hypertension Prevention Study found no significant

blood pressure lowering at 600mg per day. Investigators have analyzed their data retrospectively and found sub group and "calcium responders". These responds had a persistently lower blood pressure. An analysis to salt sensitivity has been made, but similar practical problem arises. There is no independent and prospective means of identifying those blood pressure will respond to calcium, just as there is no means of determining salt sensitivity before actually implementing therapy (or) experimental study. Hypertension has a complex etiology with multiple factors responsible for its development and maintenance. Thus it would be expected that certain subgroups of individuals might he responsive to an intervention while other would not. However there are practical limitation with respect to research and practice related to post hoc designation of responsive individuals. Design of studies of efficacy need a means of identifying possible responsiveness before initiates a trial of therapy. Similarly if only selected individuals benefit, there should be a selection and patient to receive the therapy before initiating treatment unless the therapy has seen shown to have important benefit on all potential recipients. Diuretics and other pharmacological agents have a generally beneficial effect on all treatment candidates.

Based on the data and experience available, calcium supplementation on increased dietary intake of calcium rich foods would be recommended for

treatment of hypertension non-specifically for prevention of hypertension. Some other studies are not supporting calcium therapy for treatment and prevention of hypertension, still calcium can be used because of the other benefits like prevention of osteoporosis. Therefore, a recommendation that calcium intake be maintained at 1.0 to 1.5gm per day through dietary intake on supplements on both can be made for adolescents and adults. This level should be sufficient to achieve a blood pressure lowering response in those who are responsive.

BMI and Hypertension:

In our study the mean BMI among the study group was 23.73 ± 3.28 and among the control group was 21.36 ± 2.12. The 'p' value was .00004. This shows that overweight and obesity also plays a role in the development of essential hypertension.

This was supported by a study conducted by Stamler[54]. They showed that the hypertension is about six times more common in obese than it is in lean subjects. The present study concurs with above observation. However body mass index was not related to electrolyte levels.

Similarly a study conducted by Huang stated that even a small amount of weight gain is associated with a marked increase in the incidence of

hypertension[85]. This study showed a positive correlation between BMI and blood pressure which supported our study.

In INTERSALT, the relationship between body mass index (kg/m2) and blood pressure was studied in 10,079 men and women aged 20-59, sampled from 52 centres around the world, based on a standardized protocol with central training of observers, a central laboratory and extensive quality control. Body mass index-blood pressure relationships were first studied in men and women within each centre, and results of these regression analyses were then pooled for all 52 centres. With adjustment for age, alcohol intake, smoking, and sodium and potassium excretion, body mass index was positively associated with systolic blood pressure among men in 51 of 52 centres and among women in 47, significantly so in 24 and 27, respectively. Body mass index was positively associated with diastolic blood pressure in 51 and 49 centres in men and women, respectively, significantly so in 33 and 31. Overall, a 10 kg difference in body weight was associated on average with a 3.0 mmHg difference in systolic and a 2.2 mmHg difference in diastolic pressure. In further analyses across centres, median body mass index was related significantly to median systolic blood pressure, median diastolic pressure and the prevalence of hypertension in both men and women. Body mass index was related to the slopes of systolic and diastolic blood pressure with age in women, but not in men[86].

CONCLUSION

The following were derived for our study

1. Serum Calcium was significantly less among Hypertension and correlated negatively with blood pressure.

2. In view of the significant changes Serum Calcium among Hypertensive population, community must be motivated to consume Calcium rich diet as a form of primary prevention for essential Hypertension.

SUMMARY

Essential hypertension is a major risk factor for coronary crebral and renal vascular disease. Etiology for essential Hypertension is not known many theories were postulated.

The present study attempts to focus the serum calcium level among isolated newly diagnosed essential Hypertension who were free from any other illness (or) under any medication and to correlate Sr. calcium status with the blood pressure Sr. calcium was estimated in seventy hypertensive (M= 38, F=32; mean age 53.1±5.37) & thirty health controls (M=20; f=10; mean age 51.5±5.38). Efforts were also made to final out an also between body mass index and waist circumference with systolic & diastolic blood pressure. Blood mass index was significantly more in those with stage II hypertension however it was independent of gender and Serum Calcium. Mean Serum Calcium level was significantly lower among hypertensive when compared to healthy controls. The blood pressure also correlated positively with body mass index and waist circumference where as negatively correlated with Serum Calcium.

BIBLIOGRAPHY

1. Berglund G, Anderson O, Wellebonsa L. Prevalence of primary and secondary hypertension studies in a random population sample. Br. Med Jr 1976; 2: 554.
2. MCPhee SJ, Masse BM. In: Tierney LM et al. ed. Current medical diagnosis & treatment. McGraw Hill company USA, 2006;11: 419-445.
3. Kaplan NM: Primary hypertension: Pathogenesis. In clinical hypertension. Baltimore, Williams Wilkins, 1998: 41 – 101.
4. Fisher NDL, Williams GH. In: Kasper DL et al. ed. Harrison's Principles of Internal Medicine. McGraw Hill, USA, 2005; 230: 1463 – 1481.
5. The seventh Report of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289: 2560.
6. Lopez AD, Muwaj CJL. Mortality by cause for eight regions of the world: Global burden of Disease study. Lancet, 1997; 349: 1269-1270.
7. Kearney PM, Whelton M, Raynaulds K et al. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 3665: 217-223.
8. Gupta R. Trends in hypertension epidemiology in India. J Human Hypertension 2004; 18: 73-78.

9. Stamler J, Stamler R, Neaton JD. Blood pressure systolic and diastolic, and cardiovascular risks. US population data. Arch Intern Med 1993; 153: 598-615.
10. Vanden, Hooten PCW, Feskens EJM et al, for the seven countries study research group. The relation between blood pressure and mortality due to coronary heart disease among men in different parts of the world. N Engl J Med 2000; 342: 1-8.
11. Gupta R. Defining hypertension in the Indian population. National Medical J India 1997; 10: 139-143
12. Gupta R, Sharma AK, Gupta VP et al. Increased variance in blood pressure distribution and changing hypertension prevalence in an urban population. J Human Hypertension 2000; 12: 535-540.
13. Gupta R. Trends in hypertension epidemiology in India. J Human Hypertension 2004; 18: 73-78.
14. Gupta R, Al-Udat NA, Gupta UP. Hypertension epidemiology in India: Meta-analysis and fifty year prevalence rates and blood pressure trends. J Human Hypertens 1996; 10: 465-472.
15. Gupta PC, Gupta R Rednekar MS. Hypertension prevalence and blood pressure distribution among 88,653 subjects in Mumbai, India. J Human Hypertension 2004; 18: 907-910.

16. Gupta R, Gupta S, Gupta UP et al. prevalence and determinants of hypertension in the urban population of Jaipur in Western India. J Hypertens 1995; 13: 1193-1200.
17. Kalavathy MC, Thankappan KR, Sarma PS et al. Prevalence, awareness, treatment and control of hypertension in an elderly community-based sample in Kerala, India. Med J India 2000; 12: 9-15.
18. Bharucha NE, Kuruvilla T. Hypertension in the Parsi community of Bombay: a study of prevalence, awareness and compliance to treatment. BMC Public Health 2003; 3:1.
19. Mac. Mohan S, Reto R, Cutler. Blood pressure, stroke and coronary artery disease: Prolonged difference in blood pressure: Prospective observational studies corrected for the regression dilution bias. Lancet 1990; 335: 765.
20. Jackson R, Barham P, Bills J. Management of raised blood pressure in New Zealand; A discussion document. BML 1993; 307: 107.
21. Isles CG: Prevalence, epidemiology and pathophysiology of hypertension; Oxford Textbook of Medicine, vol-2, 4th edition: 1153.
22. Illiadou A, Lichtenstein P, Morgenstein R. Repeated blood pressure measurements in a sample of Swedish twins: Heritability and associations with polymorphisms in the renin – angiotensin – aldosterone system. J Hypertens 20: 1453, 2002.

23. Harrap SP: Hypertension: Genes versus environnent. Lancet 1994; 344: 169.

24. Samani NJ; Genetics of hypertension: Oxford Textbook of Medicine, 4th edition, 2003: 1160-1164.

25. Pratt RE, Dzau VJ: Genetics and hypertension concepts, potential and opportunities. Hypertension. 1993; 33: 238.

26. Dominiazek AF, Negrin DC, Clark JS. Genes and hypertension. From gene mapping in experimental models to vascular gene transfer strategies. Hypertension, 2000; 35: 164-172.

27. Kuznetsova T, Wars J. m 2357 Angiotensin gene polymorphism and cardiovascular renal risks. J Hypertens. 1999; 17: 9.

28. Lifton RP, Gnaravi AG, Geller DS: Molecular mechanisms of human hypertension (review). Cell 104: sys, 2001.

29. Law CM, Sheil AW, Newsone LA. Fetal, infant, and childhood growth and adult blood pressure. A longitudinal study from birth to 22 years of age. Circulation 2002; 105: 1088.

30. Brenner BM, Nertow CM: Congenital Oligonephropathy. An inborn cause of adult hypertension and progressive renal injury? Curr Opin Nephrol Hypertens 1993; 2: 094.

31. Lever AF, Harrap SB: Essential hypertension: A disorder of growth with origins in childhood? J Hypertens 1992; 10: 101.

32. Pries AR, Seromb TW, Gaentgens P: Structural auto regulation of terminal vascular beds: Vascular adaptation and development of hypertension. Hypertension 1999; 33: 153.
33. Esler M, Rumantir M, Lambert G et al: The sympathetic neurobiology of essential hypertension. Am J Hypertens 2001; 14 (suppl): 139s.
34. Brunner HR, Sealy JE, Laragh JH: Renin subgroups in essential hypertension. Circ Res 1973; 32 (suppl): 99.
35. Sealey JE, Blumenfeld JR, Bell GM. On the renal basis for essential hypertension: Nephron heterogeneity with discordant rennin secretion and sodium excretion causing a hypertensive vasoconstriction – volume relationship. J Hypertens 1988; 6: 763.
36. Liese AD, Mayer-Davis EJ, Haffner SM: Development of multiple metabolic syndrome: An epidemiologic prospective. Epidemiol Rev. 1998; 20: 157.
37. Cardillo C, Killcoyne CM, Mambi S. Vasodilator response to systemic but not to total hyperinsulinemia in the human fore arm. Hypertension. 1998; 32: 740.
38. Consentino F, Luschor TF: Effects of blood pressure and glucose on endothelial function. Curr Hypertens Rep 2001; 3: 79.

39. Cardiillo C, Campia U, Kilcoyne CM. Improved endothelium – dependent vasodilation after blockade of endothelium receptors in patients with essential hypertension. Circulation 2002; 105: 452.
40. Ascherio A, Henekens C, Willet WC. Prospective study of nutritional factors, blood pressure and hypertension among US women. Hypertension 1998; 27: 1065.
41. Guyton AC: Kidneys and fluids in pressure regulation. Small volume but large pressure changes. Hypertension. 1992: 19 (suppl): 2.
42. Aperia A: regulation of sodium / potassium ATPase activity. Curr Hypertens Resp 2001; 3: 165.
43. Richards AM: The atrial natriuretic peptides and hypertension. J Inter Med. 1998; 235: 1284.
44. Mukamal KJ, Kuller LH, Fazpatrick AL, et al: Prospective study of alcohol consumption and risk of dementia in older adults. JAMA 289: 1405, 2003.
45. Thadhani R, Camargo CA Jr, Stempfer MJ. Prospective study of moderate alcohol consumption and risk of hypertension in young women. Ann Intern Med 2002; 162: 569.
46. Kannel WR, Sorte P. In: Paul O. ed. Epidemiology and control of hypertension, New York: Shafton Intercontinental Medical Book Corp, 1975; 533-592.

47. Kenronen M, Keys A. Cigarette smokers, S. cholesterol, blood pressure and body fatness. Observation in Finland. Lancet 1959; 1: 492-494.
48. Schunkert H, Koenig W, Brockel U. Hematocrit profoundly affects left ventricular diastolic filling as assessed by Doppler echocardiography. J. Hypertens 2000; 18: 1483.
49. Deverex RB, Case DB, Alderman MH. Positive role of increased blood viscosity in the hemodynamics of systemic hypertension. Am J Cardiol 2000; 85: 1265.
50. Kannel WE, Anderson K, Wilson PWF: WBC count and cardiovascular disease. JAMA. 1992; 267: 1253.
51. Cannon PJ, Stason WB, Demartini FE, et al. Hyperuricemia in primary hypertension and renal hypertension. N Engl J Med 1966; 275: 457 – 464.
52. Malhotra A, Shite DP: Obstructive sleep apnea. Lancet 2002; 360: 237.
53. Ferrier KE, Muhlmann MH, Bagret JP. Intensive cholesterol reduction lowers blood pressure and large artery stiffness in isolated systolic hypertension. J Am Col Cardiol 2002; 39: 1020.
54. Stamler R, Stamler J, Reidlinger WF. Weight and blood pressure. JAMA 1978; 240: 1607-1610.
55. Hubbard VS: Defining overweight and adiposity. What are the issues: Am J Clin Nutr. 2000; 72: 1067-1068.

56. Edwards DAW. Clin Sci 1950; 9: 259-270.
57. Blaustein M. sodium ion, calcium ion, blood pressure regulation and hypertension; a reassessment and a hypothesis. Am J Physiol 1977; 232: c165-c 172.
58. MN Chatterjea, Rana Shinde. Text book of Medical Biochemistry 5th edition 2002, Sec 4; 30: 530-531.
59. Blaustein, M.P: In zumkley H and Losse H (eds), Intracellular Elctrolytes and Arterial Hypertension. Georg Thime Verlag, New York, 1980.
60. John H. Laragh, Barny M. Brenner Hypertension pathophysiology, Diagnosis and Management 2nd Edition – 1995 Vol 1, Chapter – 70, page (1169 – 1189).
61. Knight, K.B. et al., Calcium supplementation on normotensive and hypertensive pregnant women. Am. J. Clin. Nutr. 1992 April ; 55(4) : 891-895.
62. Yamakawa, H. et al., Disturbed calcium metabolism in off spring of hypertensive parents. Hypertension 1992 Jun; 19(6 pt 1) : 528-534.
63. K. Sudhkar, M. Sujatha, S. Ramesh Babu, P. Padmavathi and P.P. Reddy. Serum calcium levels in patients with essential hypertension and their first degree relatives. Indian journal of clinical Biochemistry, 2004, 19(1) 21-23.

64. Tillman DM, Semple PF. Calcium and magnesium in essential Hypertension. Clin sci (lond), 1988 oct; 75 (4); 395-402.
65. Touyz RM, Panzv, Milne FJ. Relations between magnesium, calcium & plasma renin activity in black and white hypertension patients, miner electrolyte Metab 1995; 21 (6); 417-22.
66. Shone AC, Bookr J, Sagnella GA, Markanu ND, Macgreq GA. Serum ionized calcium and PH; effects of blood storage, some physiological influence and a comparison between normotensive and hypertensive subjects. J Hypertens, 1987 Aug; S(4); 499-505.
67. Lindl, Lithell H, Guotafsson IB, Pollare Y, Ljunshalls. Calcium metabolism and sodium sensitivity in hypertensive subject. J Hum Hypertens. 1993 Feb; 7 (1); 53-7.
68. Belizam JM, Villar J, Pinedao, Gomalez AE, Sainze, Gamera G, Sibrian R. Reduction of blood pressure with calcium supplementation in young adults Jama 1983; 249; 1161 – 1165.
69. Maccarrom DA, Morris CD. Blood pressure response to oral calcium in person with mild to moderate hypertension. Ann Intem Med 1985; 103: 825-831.
70. Cappuccio FB, markandu No, Beynon GW, shone AC, Maccnesor GA. Effect of increasing calcium intake. On urinary sodium execration in normotensive subject clin sci 1986; 76: 453 – 456.

71. Grobbee DE, hoffman A. Effect of calcium supplementation on diastolic blood pressure in young people with mild hypertension lancent 986; 2: 703 – 707
72. Nowson C, Morgan T. Effect of calcium carbonate on blood pressure. J Hynertens 1986 : 4: S 673 –S675.
73. Strazzullo P, Siani A, Guglielmis, Dicarlo A, Galltti F, Cirillom, Mancini M, Controlled trail of long-term calcium supplementation in essential hypertension 1986; 8: 1084 – 1088.
74. Ogihara T, Saito H Tabuchiy, Hashizumek Kumahona. The hypotension effect of long term oral calcium loading on elderly hypertensive patients: The importance of endogenous vitamin D3 suppression. J. Hynertens 1986; 4, S 685 – S 687.
75. Lyle RM Melby CL Hyner GC, Edmondson JW, Hiller J2, Wernberger MH. Blood pressure 2 metabolic effects of calcium supplementation in normotensive white & black man 3AMB 1981: 257: 1772 – 1776.
76. Gilliland H, Zawada ET, Mc clung D, Terwee J. Preliminary report ; natriuretic effect of calcium supplementation in hypertension women one forty. J Am Coll Nutr 1987; 6: 139 – 143.
77. Lasaridis AN, Kaisis CN, Zananiri KI, Syganis CD, Tourkantonis AA oral calcium supplementation promotes renal sodium excretion in essential hypertension J. Hypertens 1987; S : S307 – S 309.

78. Cappuccio FP, Markandu ND, singer DRJ, smith SJ, share AC, Macgnegor GA, Bes oral calcium supplementation lower high blood pressure? A double blind study J. Hypertens 1987; S: 67 – 71.
79. Siani A, Strazzullo P, Guglielmi S, Mancini M. Clinical studies of the effects of different oral calcium intake essential hypertension J Hypertens 1987: SS311 – S 313.
80. Tanji JL, Lew Ey, Wong GY, Tresuboffc, wand JA, Ansterdam A. Dietary calcium supplementation as treatment for mild hypertension. J AM board farm Pract 991: 4: 145 –150.
81. Takagi Y. Fukase M, Takatas, Fujimi T, Fusitat. Calcium treatment of essential hypertension in elderly patients evaluated by 24 H monitoring. AM J Hypertens 1991 : 4 : 836 –839.
82. Morris CD. Mccnon Da. Effect of calcium supplementation in a older population with mild increase with blood pressure AMJ Hypertens 1992; S: 230 –237.
83. Lyle RM. Does baseline serum total calcium level influence the blood pressure responsive to calcium supplementation? A double blind study Meth J Med 1992: 41 : 48 – 55.
84. the trials of hypertension prevention collaborative research group. The effect of nonpharmacologic intervention on blood pressure of person

with high normal levels. Results of the trial of hypertension prevention. Phase I. JAMA 1992, 267: 1213 –1220.

85. Huang Z, Willet WC, Manson JA: Body weight, weight change and risk for hypertension. Ann. Intern Med. 1978; 128: 81.

86. Dyer AR, Elliot P. The INTERSALT study: relations of body mass index to blood pressure. INTERSALT Co-operative Research Group. J Hum Hypertens. 1989; 3(5): 299-308.

87. Kesteloot Hugo and Geborfrs Jozer: Calcium and blood pressure, The Lancet, 10th April, 1982, 813-815.

PROFORMA

Name: Age: Sex: M / F Diet: V / NV

Address: Occupation:

SYMPTOMS:

□ Headache □ Oliguria □ Giddiness

□ Puffiness of face □ Blurring of vision □ Epistaxis

□ Swelling of legs □ Anorexia □ Chest pain

□ Vomiting / Hiccups □ Palpitation □ Easy fatiguability

□ Dyspnoea □ Polydipsia □ Polyuria

□ Bony pain □ Colicky abd pain

PAST HISTORY

□ DM □ Angina / MI □ Heart Failure

□ Renal Disorders □ PVD □ Stroke

□ Thyroid Surgery / Radiation □ Bony fracture / abnormality

PERSONAL HISTORY

□ Smoking □ Alcohol □ Drug abuse

□ Dietary milk quantity – ML

FAMILY HISTORY

□ Hypertension □ Diabetes Mellitus

ANTHRPOMETRY

Ht	cm	Wt	kg	BMI
Hip	cm	waist	cm	WHR

GENERAL EXAMINATION

Fundus	Blood pressure	
Pedal edema	Supine	Sitting
Pulse Rate	Grading of Hypertension	

SYSTEMIC EXAMINATION

CVS	RS
ABD	CNS

INVESTIGATIONS

Urine Albumin
Sugar
Deposits
Blood Glucose
Urea
Serum Creatinine
ECG
CXR PA VIEW
Serum Calcium
Corrected calcium
Total protein
Albumin
Globulin

MASTER CHART

0 – no symptom 1 – headache 2 – giddiness 3 – chest pain 4 – palpitation 5 – dyspnoea

M – male F- female; P/H – past history 1 - No 2 – Yes

Smoking 1 – Yes 2 – No; Alcohol 1 – No 2 – Yes

F/H – family history 1 – No 2 – Yes

ECG 1 – Normal 2 – LVH 3 – LAHB

Chest X ray (CXR) 1 – Normal 2 – Cardiomegaly

Fundus 0 – Normal 1 – grade I ht retinopathy

ETHICAL COMMITTEE APPROVAL LETTER

346/pharmacology
16/2/05

Ref.No. 1419/E4/3/04 Dated: 27.1.05 of the
Dean, Govt. Rajaji Hospital, Madurai.

Minutes of the First Ethical Committee Meeting for the year 2005 held at 12.30 P.M. on 2.2.05 at the Deans Chamber, Govt. Rajaji Hospital, Madurai.

The following members of the Committee were attended the meeting.

1) Dean incharge/Chairman of Ethical Committee
2) Prof. of Medical Oncology
3) Prof. of Surgical Oncology
4) Prof. of Obst. & Gynaecology
5) Director, Institute of Pharmacology
6) Prof. of Opthalmology
7) Prof. of Medicine.

The member of the Ethical Committee approves the following projects.

Name	Project	Remarks
1. Prof. and H.O.D. Dept. of Medicine Govt. Rajaji Hospital	Histopathologic studies of nature valves from autopsy samples	Approved/Permitted
2. Prof .and H.O.D. Dept. of Medicine Govt. Rajaji Hospital, Madurai.	Bullying among Medical students	Not permitted
3. Prof. and H.O.D. Dept. of Obst. & Gynaec. Madurai Medical College, Madurai.	ICMR Study on Randomised Controlled Clinical Trial with Praneem Polyherbal Tablet and Standard treatment for abnormal Vaginal discharge.	Approved/Permitted
4. Prof. and H.O.D. Dept. of Medicine Madurai Medical College, Madurai	Dietary and anthro pomatic aspects among patients with coronary heart diseases	Approved/Permitted
5. Dr.C.Ravindranath Asst. Prof. of Psychiatry. Govt. Rajaji Hospital, Madurai.	Psychiatry Morbidity in l Medica Oncology	Approved/permitted
6. Dr.S.Kanatha Pandian Reader and Head of Bio Tech. Alagappa University. Karaikkudi	To obtain bacterial and fungalsamples from Opthalmology department,. GRH., Madurai	Approved/permitted

02266

7. Dr.K.Raadhika P.G.Student, Pharmacology, Madurai Medical College, Madurai.	Bronchodilators in bronchial Asthma.	Approved/permitted
8.Dr.V.Theivanai. P.G.Student, Pharmacology Madurai Medical College, Madurai	Pharmacological challenges in Anti-Retro viral Therapy	Approved/permitted
9. Dr. V.Anand. P.G.Student in M.D) (General Madurai Medical College, Madurai.	Serum Calcium level in newly diagnosed Hypertension	Approved/permitted
10. Prof. and H.O.D. of Medicine, GRH, Madurai.	Identification of slow and rapid acetylators among T.B. population	Approved/permitted
11. Mr. Minashi Kumar Mr.Girhani Lal Dayal III MBBS., MMC, Madurai	Congenital Heart diseases in ICMR & RC,GRH, Madurai.	Approved/permitted
12. Prof and H.O.D. of Medicine, Govt. Rajaji Hospital, Madurai	Mortality study in Primary Hyperoxaluria	Approved/permitted

ndt. No. 2266/E1/4/05 Dt. 15.02.2005.

Note:

1) All those are doing project or research work are instructed to submit a detailed summary of their work to the ethical committee on completion of the work.
2) All those who are involved in their work should duly acknowledge the ethical approval in their work.
3) The project or research work should be limited for which the ethical committee has given approval.
4) They should not violate ethical approval and limits/regulations.
5) If any modification is not approved, requires a fresh application.

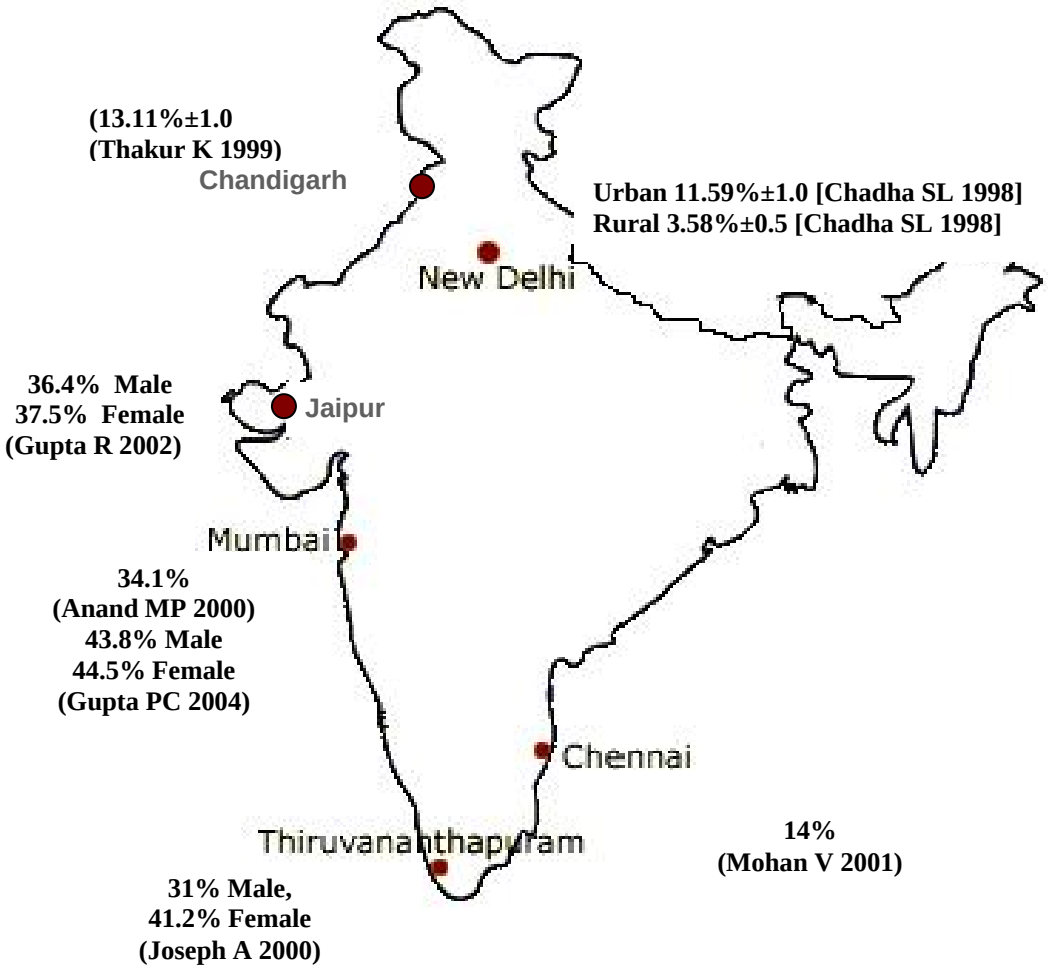
FORWARDED /

ADMINISTRATIVE OFFICER
Madurai Medical College
Madurai - 625 020.

DEAN/CHAIRMAN
Ethical Committee
Govt. Rajaji Hospital,
Madurai.

To
Dr. V. Theivanai
P. G. Student
Pharmacology
Madurai Medical College - Thro. Proper Channel.

Fig. 1 Prevalence of hypertension in India over the years 1998-2004*



*** Source:** Gupta R: Trends in Hypertension epidemiology in India: J Hum Hypertens 2004: 18; 73-78.

Fig – 1

Distribution of cases and controls in relation to age

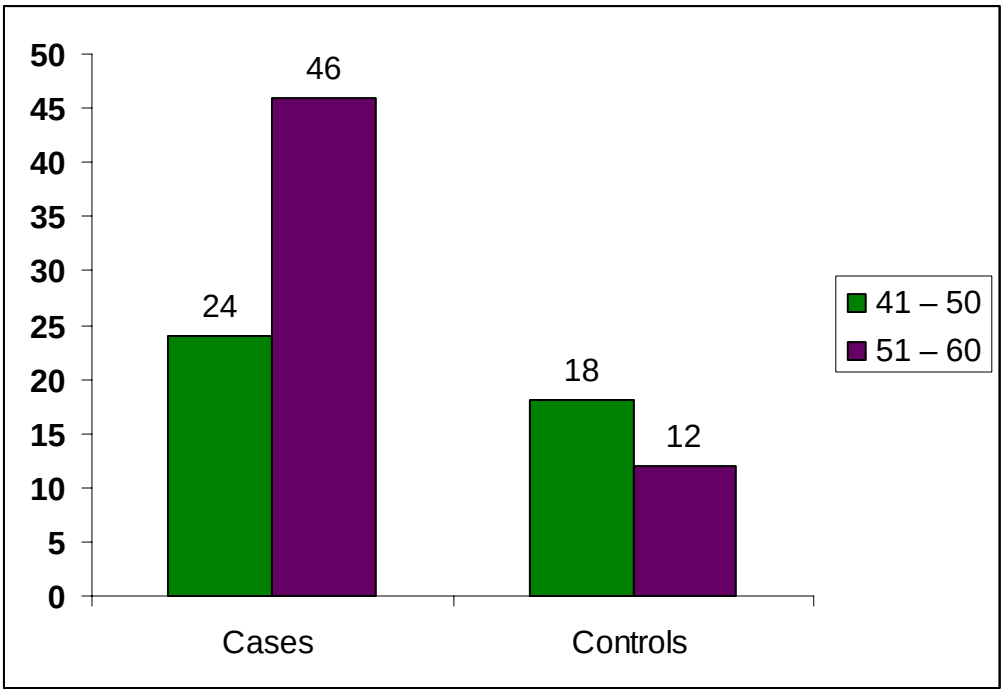


Fig – 2

Distribution of cases and controls in relation to gender

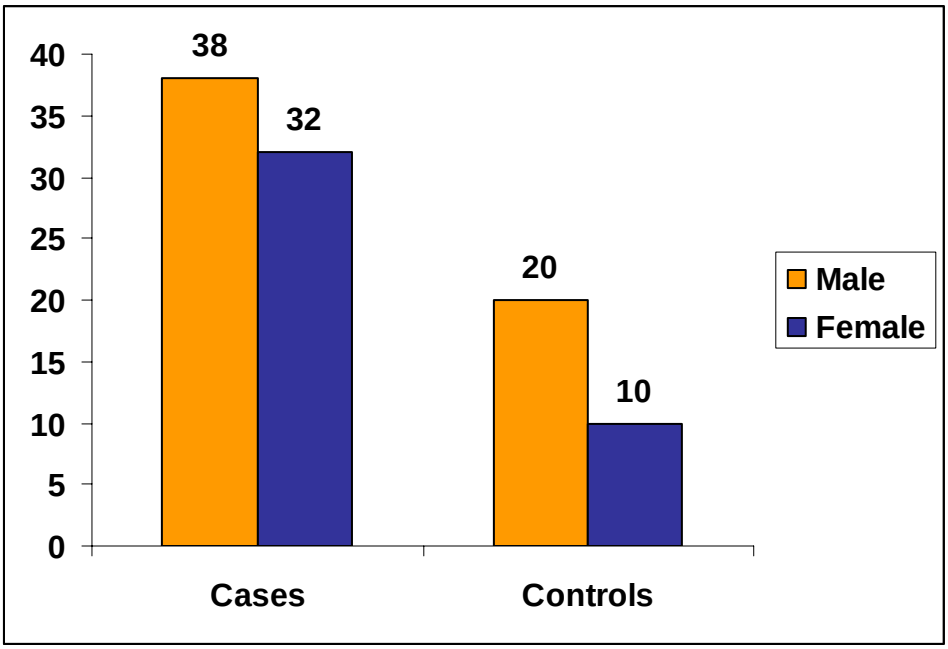


Fig – 3

Distribution of cases and controls with respect to

Body Mass Index (BMI)

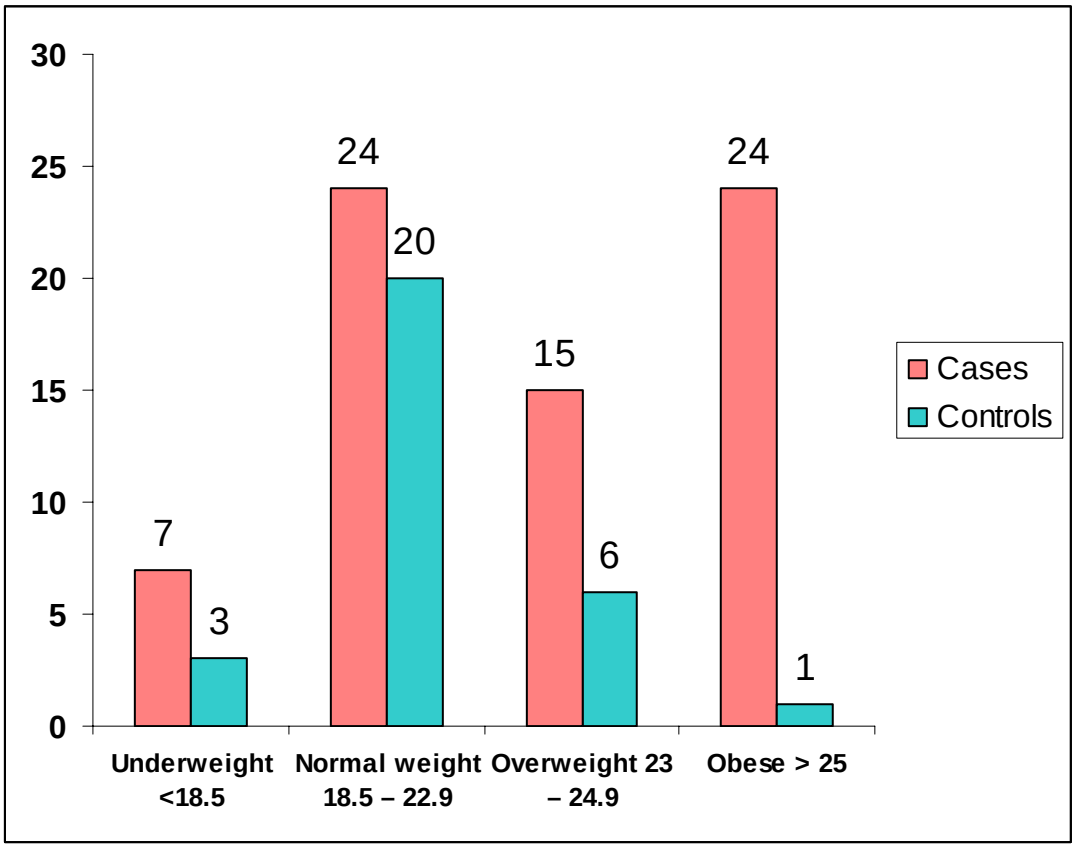


Fig – 4

BMI among cases and controls

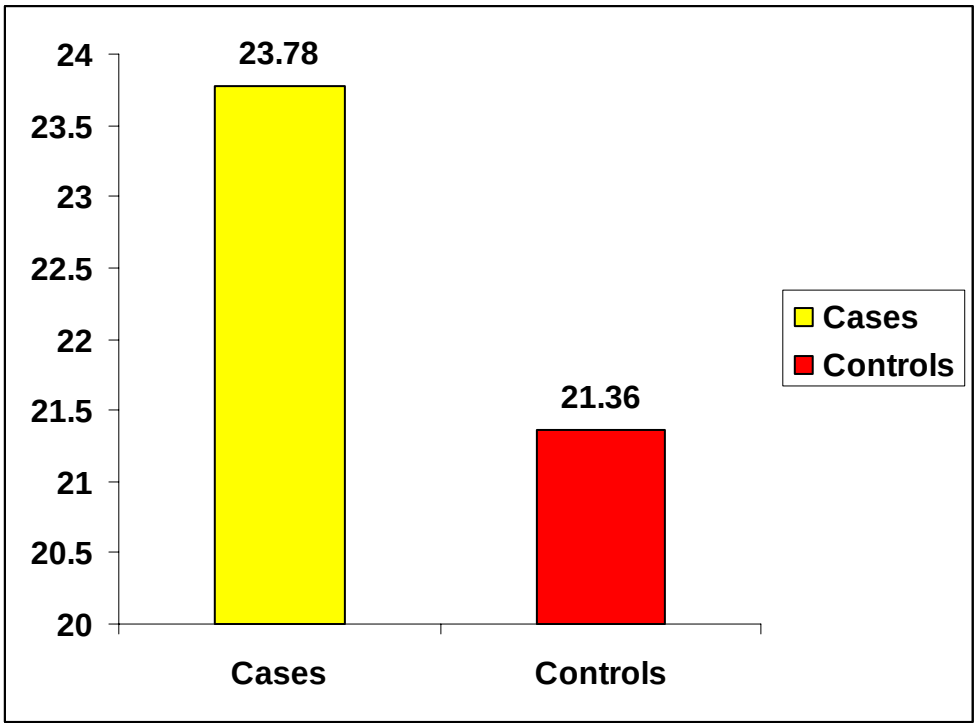


Fig – 5

BMI of cases and controls with respect to gender

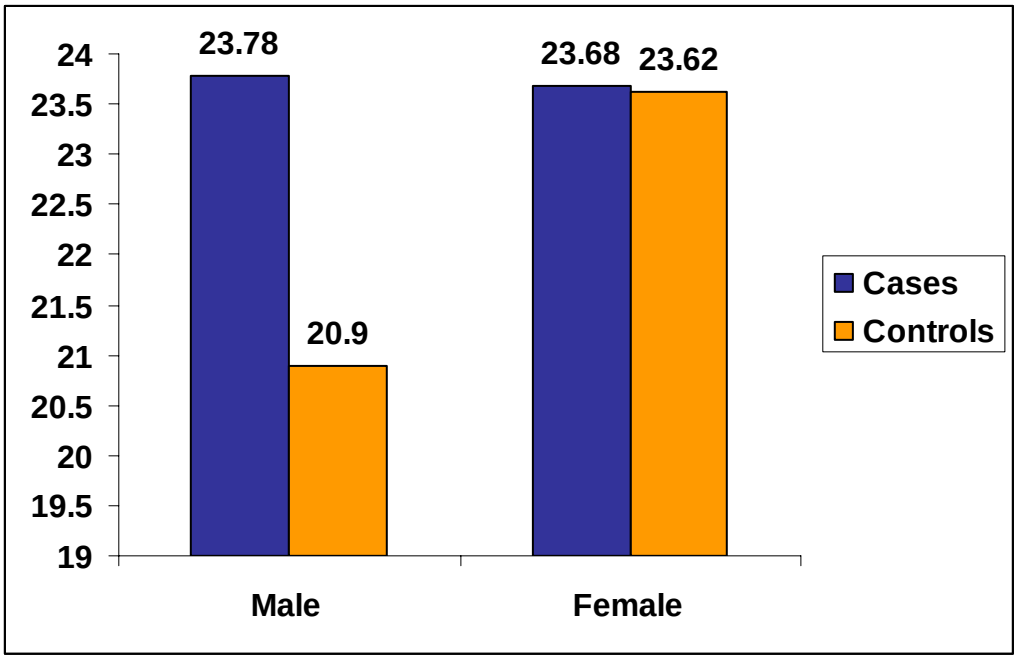


Fig – 6

BMI with respect to Hypertension

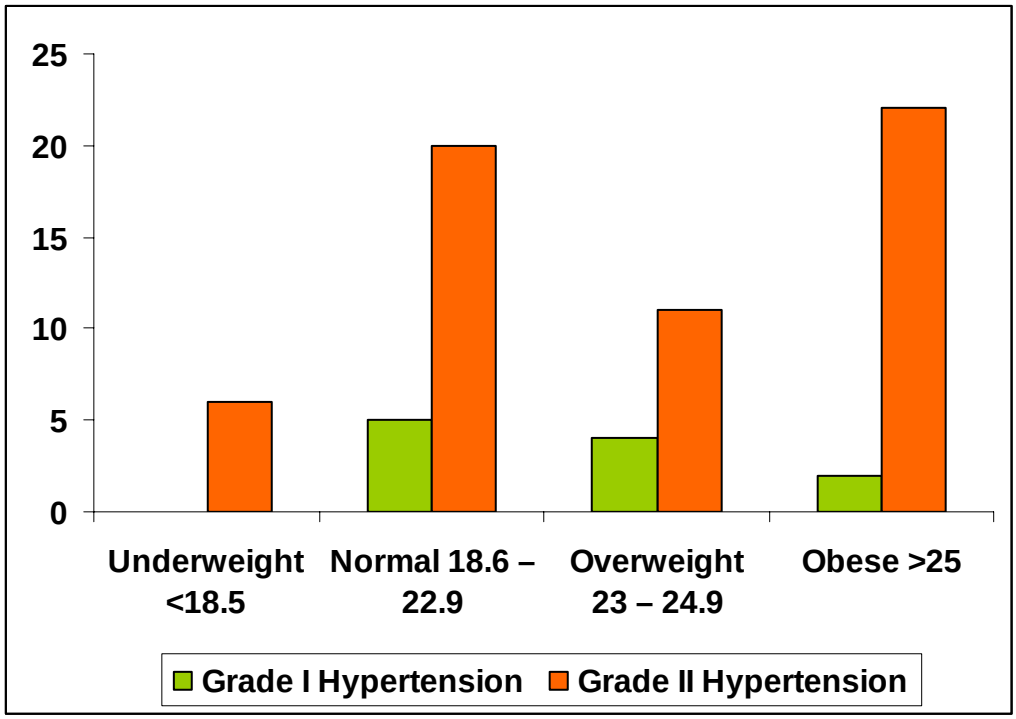


Fig – 7

Analysis of presenting symptoms

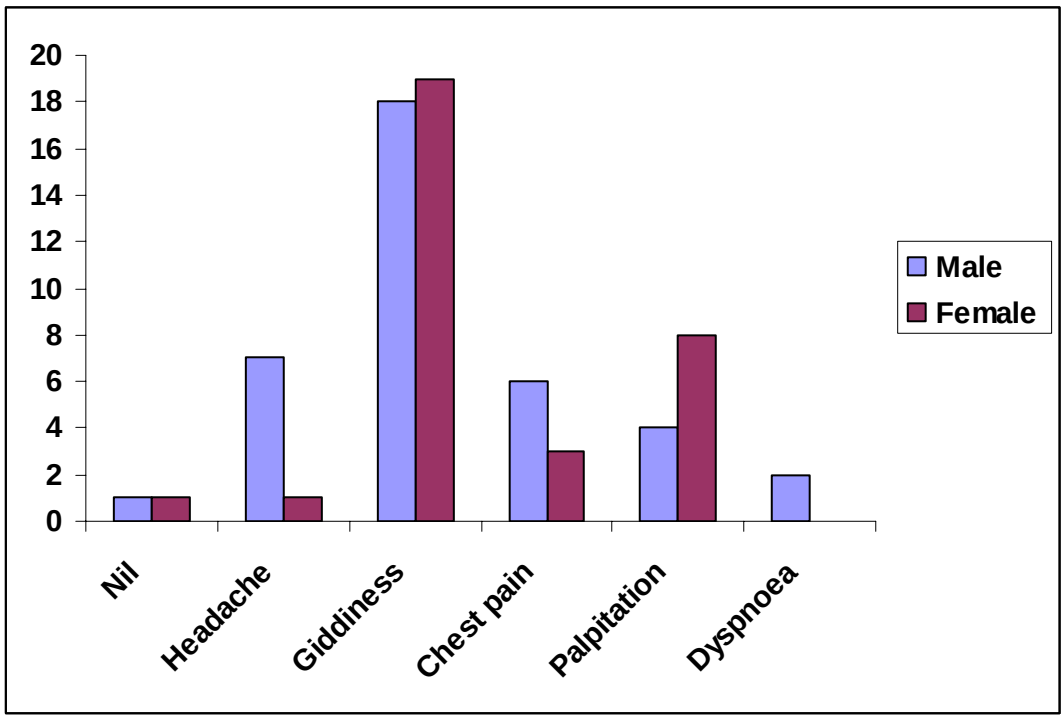


Fig – 8

Distribution of systolic and diastolic blood pressure

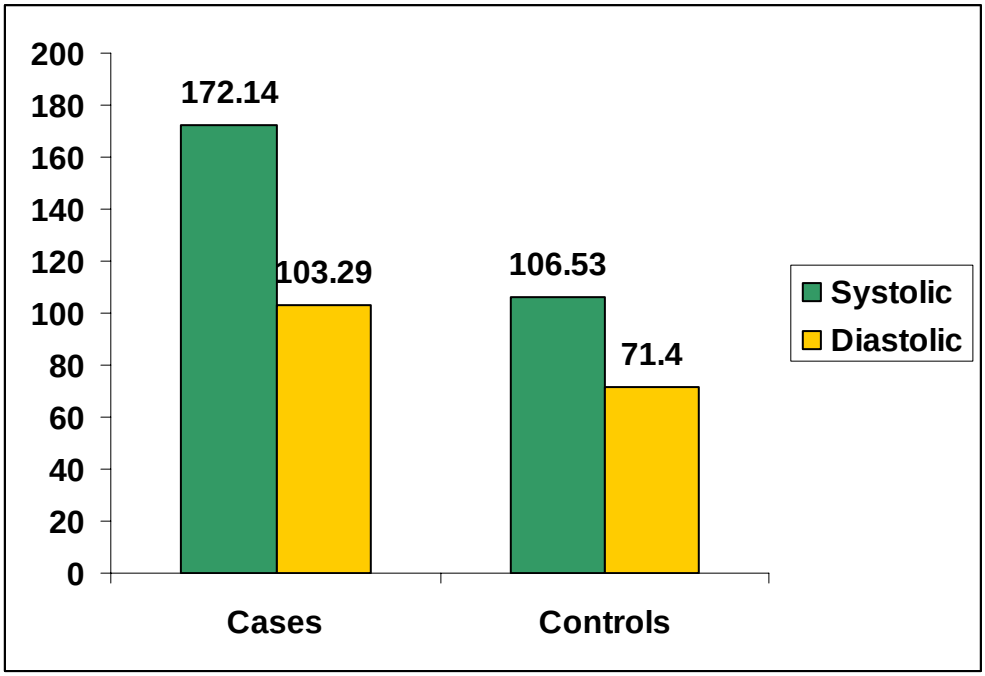


Fig – 9

Distribution of cases with respect to grading of hypertension

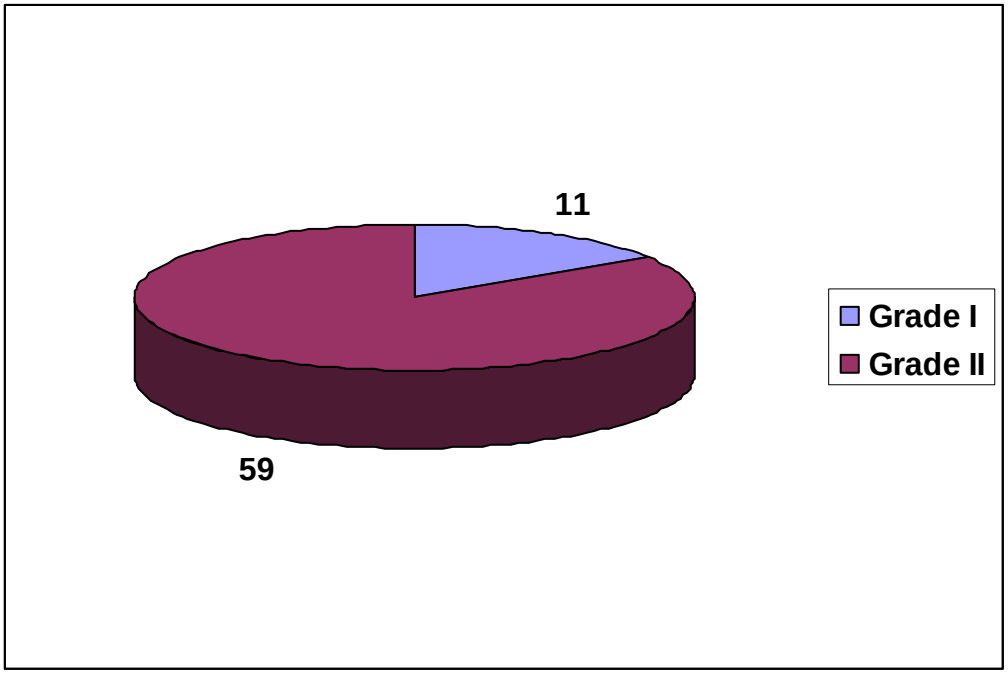


Fig – 12

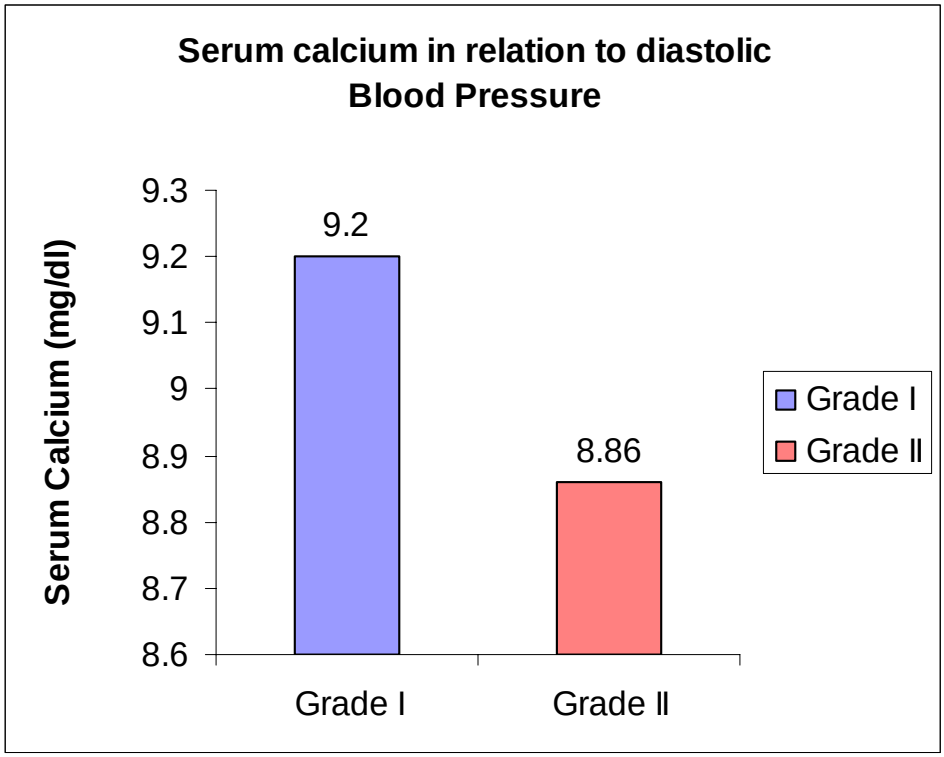

Serum calcium in relation to diastolic Blood Pressure
Serum Calcium (mg/dl)
9.3
9.2
9.1
9
8.9
8.8
8.7
8.6
9.2
8.86
Grade I
Grade II
Grade I
Grade II

Fig – 11

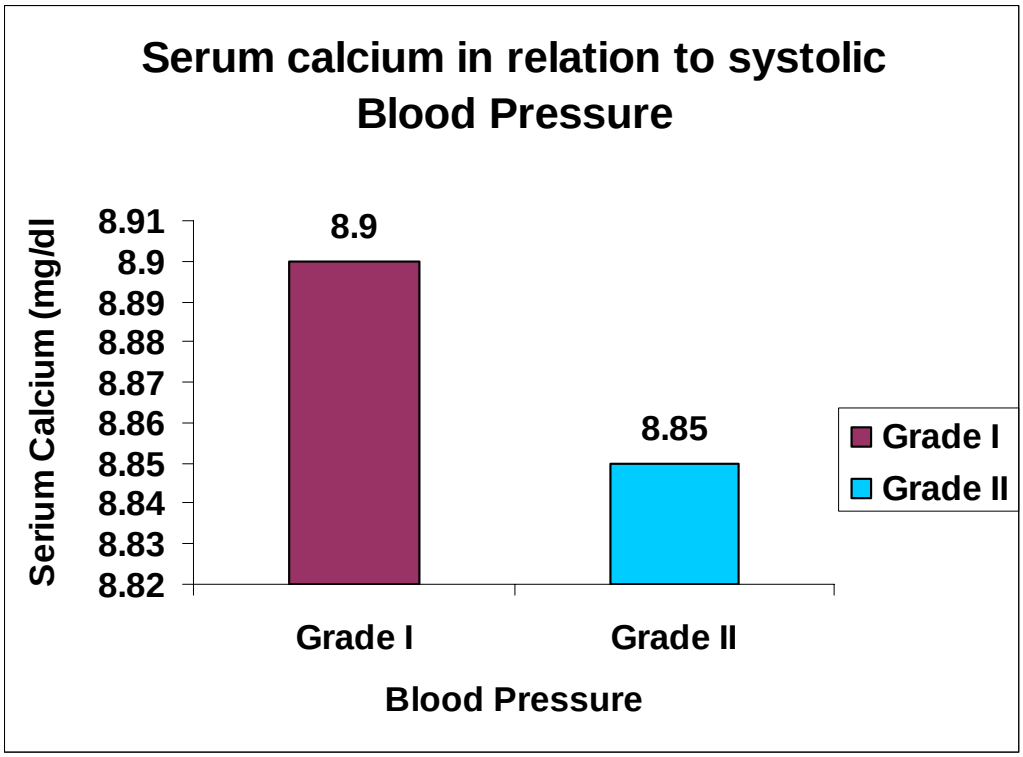
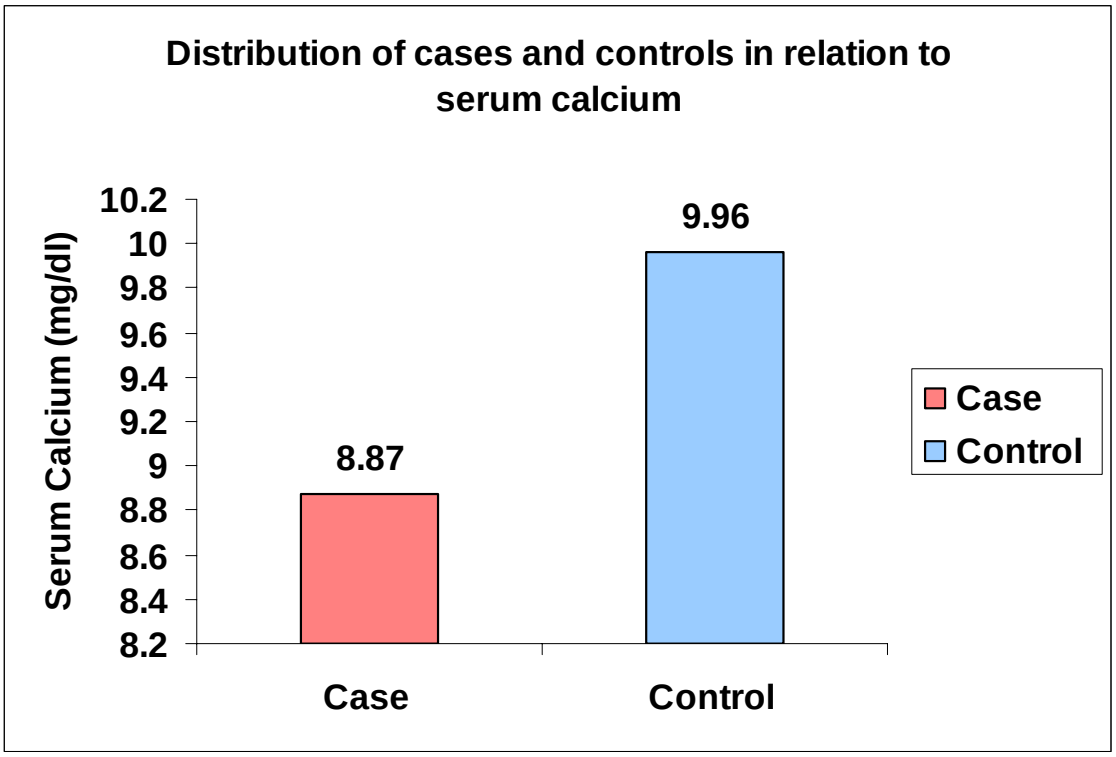

Serum calcium in relation to systolic Blood Pressure
Serium Calcium (mg/dl
8.91
8.9
8.89
8.88
8.87
8.86
8.85
8.84
8.83
8.82
8.9
8.85
Grade I
Grade II
Grade I
Grade II
Blood Pressure

Fig – 10


Distribution of cases and controls in relation to serum calcium
Serum Calcium (mg/dl)
10.2
10
9.8
9.6
9.4
9.2
9
8.8
8.6
8.4
8.2
8.87
9.96
Case
Control
Case
Control